COMBINATION PRODUCTS SUMMIT

COLUMBUS, OH • NOVEMBER 7–9, 2022

Bridging between Combination Product Drug Delivery Device Presentations: Strategies to leverage data and minimize patient burden

Ryan McGowan, AstraZeneca

Jiaying Shen, Merck

John McMichael, AstraZeneca

AFDO RAPS HEALTHCARE PRODUCTS COLLABORATIVE

AFDO RAPS

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Workshop Overview

Ryan McGowan
CMC Regulatory Affairs,
AstraZeneca

Introduction and Combination Product Bridging Overview
Overview of key combination product bridging concepts and definitions and review of 2019 the US FDA issued a draft guidance on “Bridging for Drug-Device and Biologic-Device Combination Products”

Jiaying Shen
Medical Device and Combination Product Development, Regulatory and Quality, Merck

Combination Product Bridging Toolbox
Presentation of available combination product bridging tools and recommendations for when the bridging tool is most appropriate through presentation of real-world case studies.

John McMichael
CMC Regulatory Affairs,
AstraZeneca

Bridging Challenges in Case Studies and Tabletop Group Activity: Working Through Bridging Scenarios
Review of combination product bridging challenges via several case studies across the parenteral and inhalation drug delivery spaces and group exercises.

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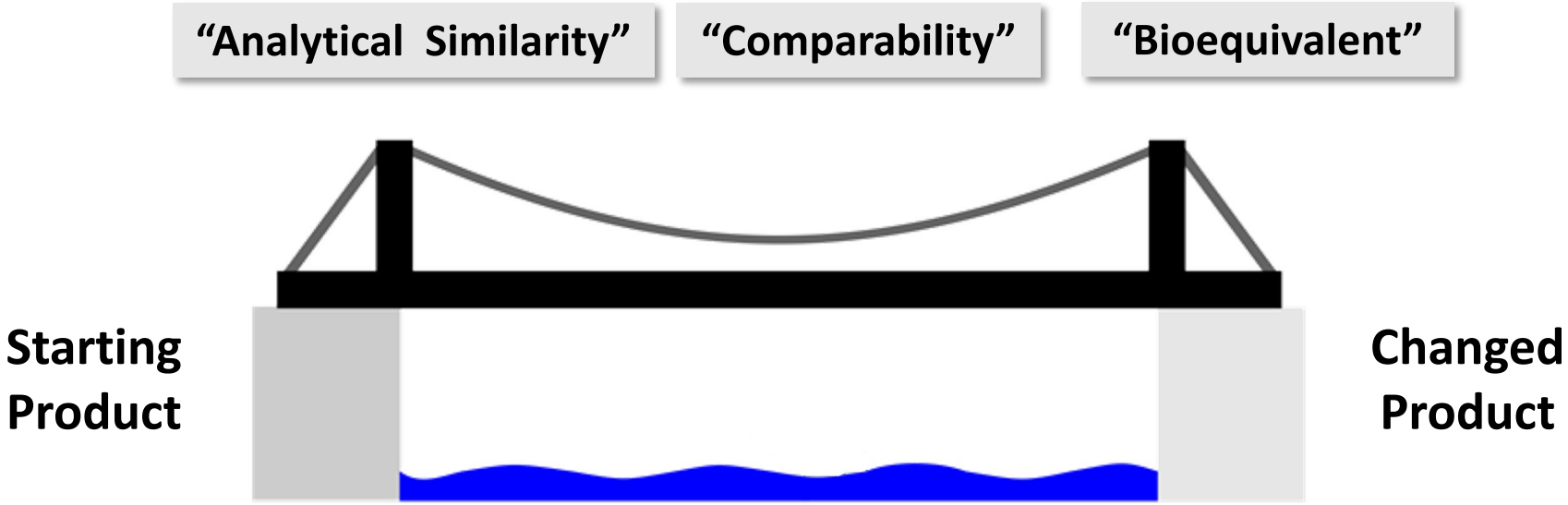
Introduction and Combination Product Bridging Overview

Ryan McGowan, AstraZeneca

Nov. 2022

Bridging Concepts and Definitions

The medical device and pharmaceutical industries have historically applied the concept of “bridging” between product versions and process changes.



Bridging Concepts and Definitions

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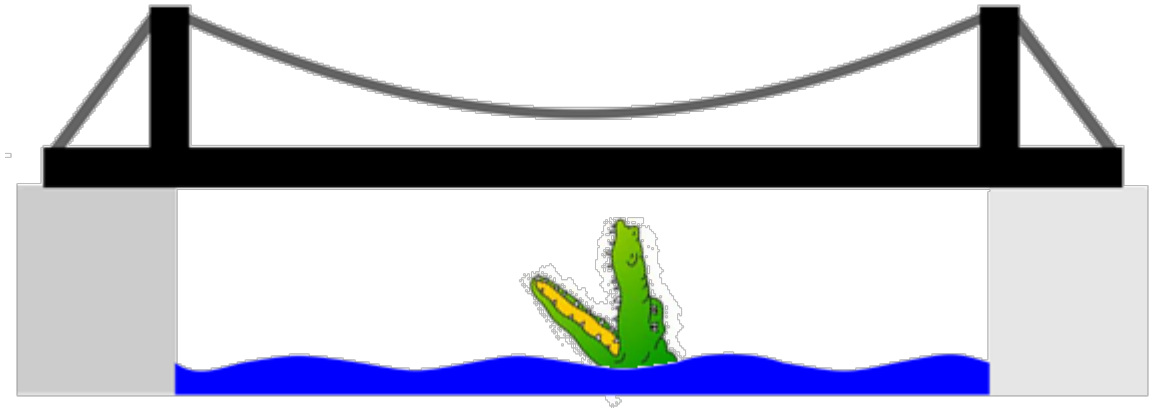
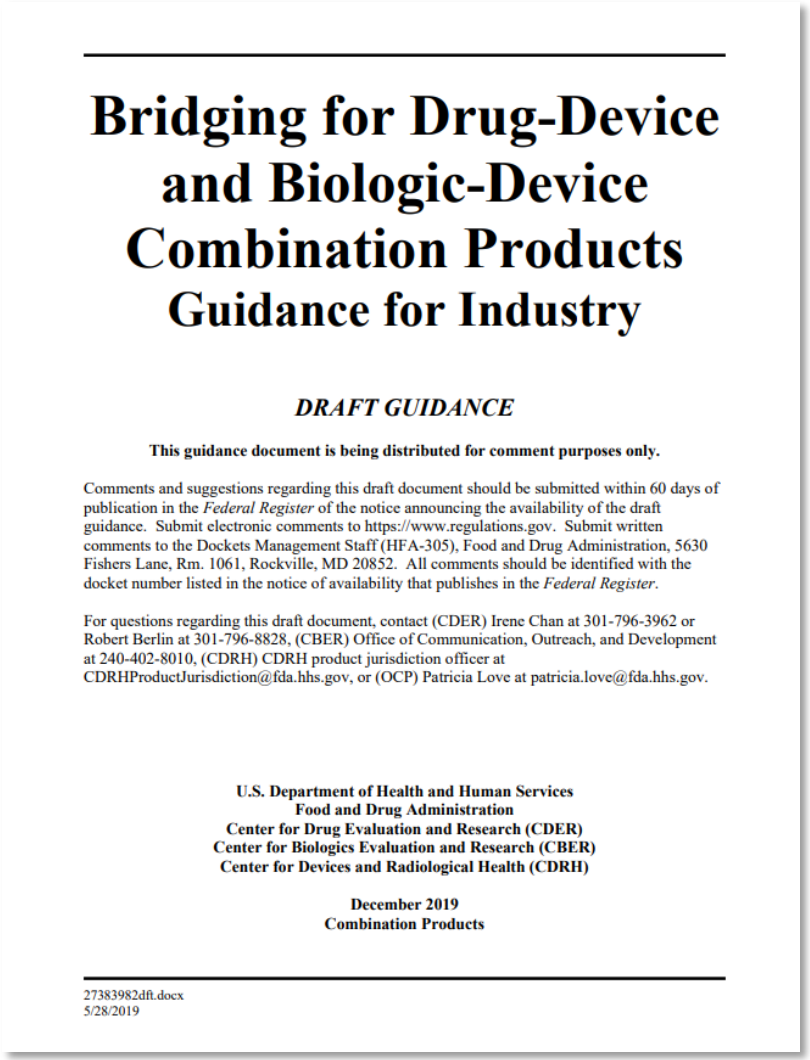
Starting Product



Changed Product

Unnecessary Data Generation

Bridging Concepts and Definitions



Bridging for Drug-Device and Biologic-Device Combination Products
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 https://www.regulations.gov. Submit written comments to the Dockets Management Staff (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) Irene Chan at 301-796-3962 or Robert Berlin at 301-796-8828, (CBER) Office of Communication, Outreach, and Development at 240-402-8010, (CDRH) CDRH product jurisdiction officer at CDRHProductJurisdiction@fda.hhs.gov, or (OCP) Patricia Love at patricia.love@fda.hhs.gov.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

December 2019
Combination Products

27383982dft.docx
5/28/2019

The term bridging refers to the process of establishing the scientific relevance of information developed in an earlier phase of the development program or another development program to support the combination product for which an applicant is seeking approval.

Once the applicant has established the relevance of such information to (i.e., bridged to) its product, the applicant can leverage that information to streamline its development program.

Bridging Concepts and Definitions

5 Step Process for Successful Bridging Strategy – FDA Draft Guidance

"Successful Bridging Strategy"

Golden Gate Bridge[1]
1937 - Present

"Unsuccessful Bridging Strategy"

Tacoma Narrows Bridge[2]
July 1940 – November 1940

[1] – Source: https://giphy.com/explore/goldengate-bridge
[2] – Source: http://retronewser.com/2020/11/07/caught-on-camera-tacoma-narrows-bridge-in-washington-collapses/

Bridging Concepts and Definitions

5 Step Process for Successful Bridging Strategy – FDA Draft Guidance

Identify all differences between the prior and new product presentation/process and consider the potential effect of differences on the safety and effectiveness profile.

Identify existing information that has been gathered or generated through studies and assessments for the prior product and compare it to the safety and effectiveness submission requirements necessary for approval of the new product.

Identify and explain how and why existing information for the prior product / process can be bridged and leveraged to support approval of the new product.

Focus on any information gaps remaining and consider whether other existing information can be reviewed and used to address these gaps.

Compare findings from Step 2 through 4 and identify the remaining gaps in information that need to be addressed for approval of the new product/

Common Bridging Tools

- **Benchtop / Analytical Testing** – Engineering or chemistry assessment comparing objective attributes before and after a presentation change
- **Pharmacokinetic Assessment –** Clinical study measuring the drug exposures within the body and assessing the drug delivery characteristics before and after a presentation change
- **Human Factors Studies –** Simulated use study assessing the use risks and critical tasks of the new presentation and ensuring the new system is safe for use
- **“Actual Use” / “Real world patient handling” Studies –** Clinical studies assessing safety, success in drug delivery, and robustness of the new presentation

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Common Bridging Tools

- **Benchtop / Analytical Testing** – Engineering or chemistry assessment comparing objective attributes before and after a presentation change

  Common in CMC changes with container closures. Expanded scope when combination product is involved.

- **Pharmacokinetic Assessment –** Clinical study measuring the drug exposures within the body and assessing the drug delivery characteristics before and after a presentation change

  Common in CMC / clinical presentation changes. Combination products add another dimension (ensuring drug delivery remains the same)

- **Human Factors Studies –** Simulated use study assessing the use risks and critical tasks of the new presentation and ensuring the new system is safe for use

  Unique to combination product bridging, but in many cases these data are already collected for new products / significant changes in product

- **“Actual Use” / “Real world patient handling” Studies –** Clinical studies assessing safety, success in drug delivery, and robustness of the new presentation

  Unique to combination product bridging and can be challenging….

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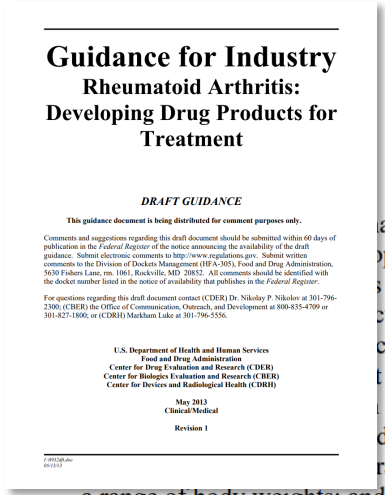
Unique to medical device bridging and very challenging….

Real World Patient Handling Programs



Guidance for Industry
Rheumatoid Arthritis: Developing Drug Products for Treatment

DRAFT GUIDANCE

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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)

May 2013
Clinical/Medical

Revision 1

arketed formulation and drug-device combination product
ptimal, we acknowledge that changes to the drug product delivery
s in the formulation, excipients, or device components may affect the
cteristics and clinical performance of the drug-device combination
cal data needed to support such changes depends on the nature of the
t stage. For example, a transition from a prefilled syringe to an
involves the following, at a minimum: (1) human factor studies to
d risks of the modified combination product; (2) a pharmacokinetic
rates similar delivery of the drug product to the same biospace across
a range of body weights; and (3) real-life patient handling experience to assess device performance as discussed above. Depending on the extent of the proposed changes, additional clinical data may be needed to support efficacy and safety, including immunogenicity.

Clinical studies assessing safety, success in drug delivery, and robustness of the new presentation. Typical endpoints:

- Patient-reported injection success (e.g., diary)
- Pharmacokinetic values (e.g., blood draw)
- Safety of patient / caregiver
  (e.g., injection site reaction, needle stick)

Generally, ~150-200 patients

Consider these studies with caution:

- Not included in FDA's draft guidance on combination product bridging
- PK studies may be better tools for measuring any unique safety events (e.g., injection site reaction)
- Human Factors studies is a better tool to identify use risks, root causes, and mitigations
- May be appropriate for new, complex, device type that does not have clinical data (e.g., body worn injectors)

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Combination Product Bridging Case Studies

Jiaying Shen, Merck

Nov. 2022

Disclaimer

- The views presented here are my personal views and not necessarily those of Merck as an organization

Understand the Basics 1

- As a lead in the R& D function, some comment questions/observations about the FDA bridging guidance while sitting on review committee:
  - Scope – clinical vs commercial
    - Applicable to both phases
    - FDA encourages the applicant to conduct clinical studies using the device constituent parts with which it intends to market the combination product. By doing so, bridging to clinical data likely would not be needed because the data would have been developed with the final finished combination product
  - Scope – what information can be used
    - Information from an earlier phase of the development program or another development program

Understand the Basics 2

- Confusion between **Bridging** and **Leveraging**
  - The term bridging refers to the process of establishing the scientific relevance of existing information to support the combination product that is seeking approval
  - Then the applicant can leverage that information to streamline its development program
- Mix of three categories of existing information
  - Drug/Bio product agnostic info
  - Information that can be bridged and leveraged
  - Data recollected with the same methods
- Following this bridging guidance does not eliminate the need to contact FDA to discuss specific information needed to support applications
- Demonstrating compliance with the bridging guidance can make the review process easier

Understand the Basics 3

Guidance (Ideal)

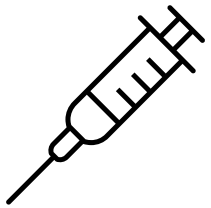
1. Different device constituent part or parts with the same drug constituent part or parts
2. Different drug constituent part or parts with the same device constituent part or parts

Reality

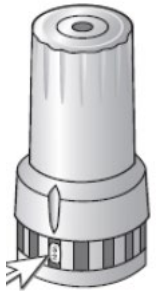
1. Drug formulation might have some changes
2. Device constituent parts are not the same

Need to bridge some device and drug features at the same time

Impact on Drug Performance



VS



Early Phase ► Pivotal ► Commercial

Case Studies

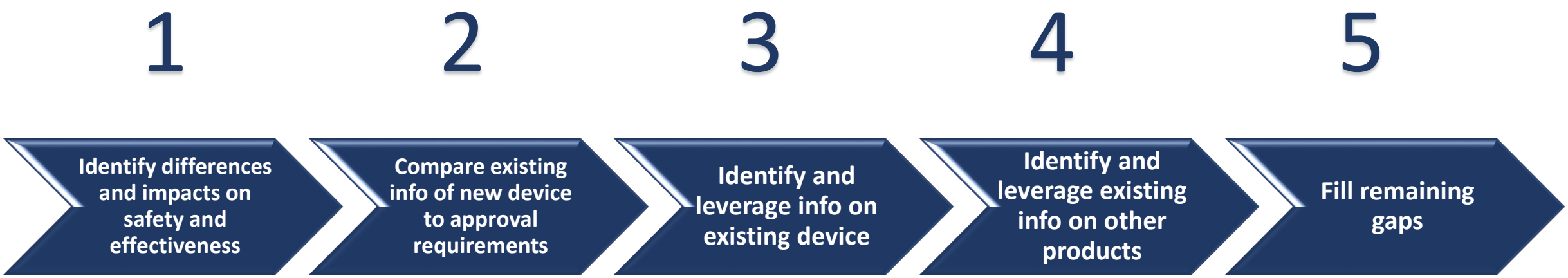
- Two cases will be presented
  - Multi Dose Pen Injector
  - Prefilled Syringe

Multi-Dose Pen Injector

Pivotal ► **Commercial**

- Phase 3 device is a marketed reusable multi-dose pen injector (with 501K clearance)
- Commercial device is a single use multi-dose pen injector
- The same drug in the same cartridge
- Identical injection needles are used

Five Steps Bridging Process



Step 1: Identify Differences and Impacts on Safety and Effectiveness

Device Changes	Impacts
User Interface not Identify	Whether product can be used safely and effectively
Device Design	Drug delivery related functionality (dose accuracy, dialing force and injection force etc.).
Manufacturing process	Drug quality: stability/degradation
	CMC considerations: e.g. device functionality, sterility throughout shelf life, and expiration dating

Step 2: Compare Existing Info to Approval Requirements

- For commercial pen injector, full design control applied, including
  - Design requirements
  - Design verification tests
  - Device risk management work
  - Biocompatibility
  - Process validation
  - Human factors work
  - Compatibility/sterility

- What is missing – the commercial pen injector was not tested in the pivotal clinical study

Step 3/4: What can be bridged and leveraged

What Remains the Same	What can be Bridged and Leveraged
Drug concentration, drug viscosity or formulation	• Local injection adverse reaction profile • Bioavailability of the drug and/or its metabolic profile • Leachable and extractable profiles
Drug Cartridge	
Route of administration	
Needle depth/Tissue plane/Rate of Infusion	

Step 5: What Gaps to address

- How the existing clinical pen injector data be bridged and leveraged?
  - Detailed Form and Functional Attributes Comparison
  - How the observed clinical pen injector related events be addressed in the marketed pen injector

- Result:
  - Obtained approval without additional data requested by the agency

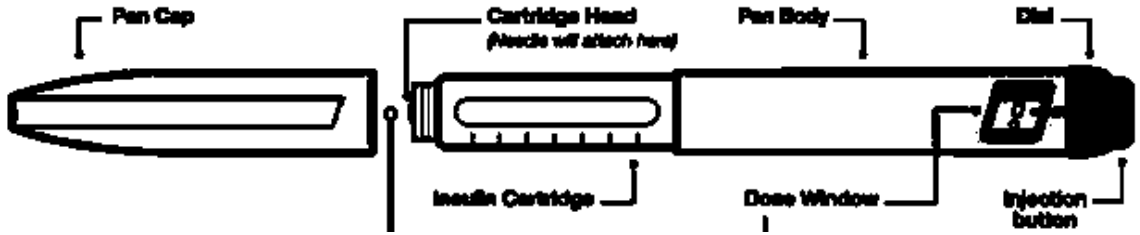
Form and Functional Attributes Comparison

- How to do it?
  - Device form
  - User interaction

Device Form Similarity and Difference	Preparation of the Pen	Dose Setting	Dose Delivery	Completing Use of the Pen

Pictures of Pen Injectors

- Reusable multi-dose
- Single multi-dose



Similarities in Key Features and Functions

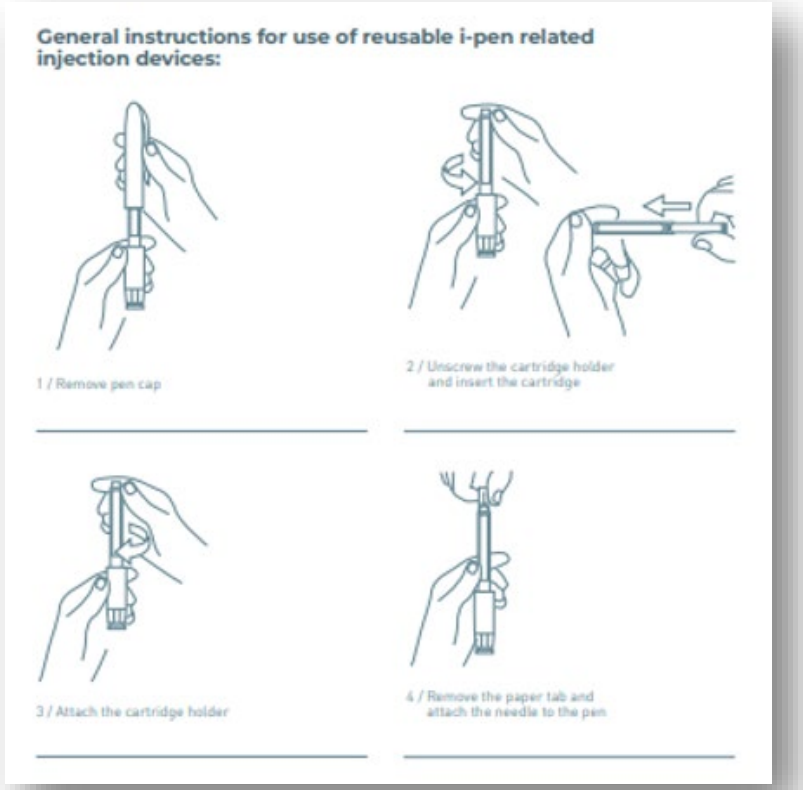
- The same drug path features/functions:
  - The same drug in the same cartridge
  - Identical injection needles are used
  - The same injection process - needle attaching/detaching, priming, dose setting correcting, injection
- Identical dose setting range and resolution (the same maximum dialable units in 1 unit increment).
- No stored energy or automated functions are involved in any of the device functions
- Tactile and audible feedback provided during dose setting.
- The set dose is displayed in a dose window on the body of the injector below the dose window
- Dose accuracy achieved across dose setting range in accordance with ISO 11608-1.
- Indicator scale of remaining contents in the pen injector

Comparison of Attributes Relevant to Device Form

- Material
- Dimensions
- Shape
- Color
- Pen cap to cartridge holder attachment orientation
- Dose display location
- Markings – remaining content scale
- Inspection windows
- Septum opening
- Threaded connection
- Dose knob design
- Height above dose knob when depressed for injection
- Dose display appearance
- Dose scale numbering
- Dose scale font size
- Injection stroke distance
- End of injection stroke indication

Comparison of Attributes Relevant to Preparation of Use

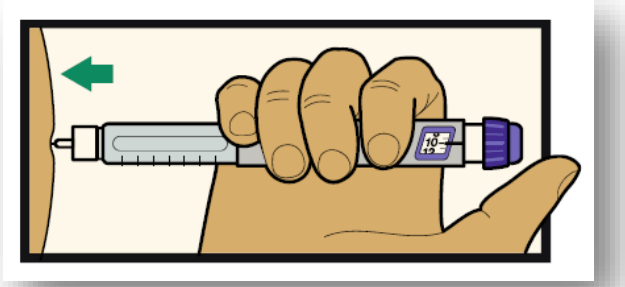
- **Pen cap removal force –** minimum and maximum cap removal force
- **Loading of the drug product cartridge -** preassembled vs user loaded
- **Pen needle compatibility –** follow the latest ISO 11608-2 standard
- **Pen needle operation –** how to attach



Comparison of Attributes Relevant to Dose Setting

- **Dialing Direction -** turning the dose knob clockwise/counter clockwise
- **Dialing Range/Dialing Resolution -** minimum/maximum dialable dose ; dialing increment
- **Dialing Torque -** minimum/maximum torque required to set a dose
- **Dialing Feedback -** Device signals during dose setting (visible, audible, tactile)
- **Maximum dose stop torque -** torque required to overcome the position “maximum dose” of the dose sleeve clockwise
- **Last Dose Stop Torque -** torque required to overcome the "last dose" position of the dose sleeve

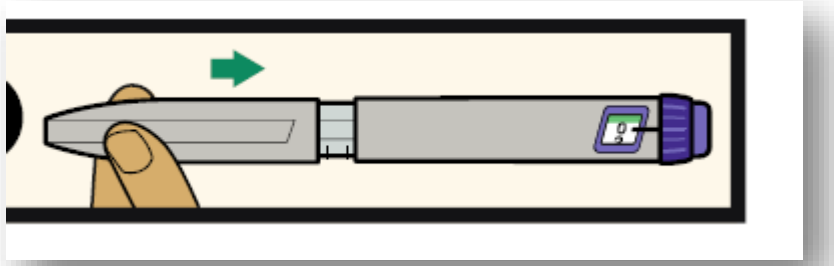
Comparison of Attributes Relevant to Dose Delivery



- **Needle insertion –** dart like motion; via one-handed operation
- **Injection actuation –** push the dose button
- **Injection mode -** manual
- **Injection stroke force -** required force on the dose button to operate the drug delivery functionality
- **Injection dose accuracy -** Dose accuracy for delivery of the contents contained in the cartridge must meet requirements as stipulated in ISO 11608-1
- **Injection stroke feedback -** Device signals during dose injection (visible, audible, tactile) should be detectable by the user in a typical use setting with typical background noise and lighting experienced in the average home setting, hospital or healthcare provider office

Comparison of Attributes Relevant to Completing Use of the Pen between Clinical and Commercial Pen Injectors

- **Pen cap attachment force –** The minimum and maximum force to attach the pen cap
- **Pen needle operation –** how to detach



Clinical Use Events

The clinical pen injector was used in two clinical studies.

A total of six (6) complaints were received during the conduct of the clinical studies. All complaints were related to device stalling and/or sticking during mid injection:

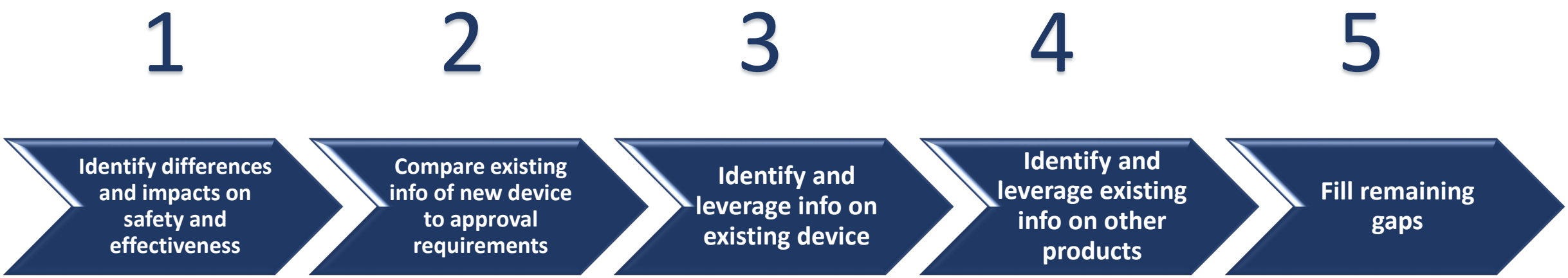
"Patient describes that the plunger would get stuck mid-injection"	"The plunger on the Tactipen would get stuck mid injection. The dosing was not affected in any way."	"Patient reported that the plunger mechanism would stuck mid-injection"
"Patient describes that the plunger would get stuck mid-injection"	"Patient reported that the plunger mechanism would stick during injection"	"Patient describes that the plunger would get stuck mid-injection"

Early market research showed similar observations on "stalling" or "sticking" during the injection stroke. Design changed were made, such as increasing the height above dose knob when depressed for injection

Prefilled Syringe (PFS)

- For the product under development (product A), the same PFS is used for both clinical and commercial
- The same or similar PFS are approved for two other products (product B and C)
- Product A plans to use the same filling and assembly equipment as Product B and C

Five Steps Bridging Process



Step 1: Analysis

Characteristics	Product A	Product B	Product C	Discussion of Differences
Dosage form	Prefilled Syringe	Prefilled Syringe	Prefilled Syringe	No difference
Route	Intramuscular administration only	Intramuscular administration only	Intramuscular administration only	No difference
Volume	0.5ml	0.5ml	0.5ml	No difference
Indications	X	Y	Z	Different
Intended user groups	Healthcare Professionals	Healthcare Professionals	Healthcare Professionals	Some difference
Use environment	Clinical setting	Clinical setting	Clinical setting	No difference

Step 1: Analysis Results

Changes	Impacts
Drug concentration, drug viscosity or formulation	Local injection adverse reaction profile
	Dose Accuracy
	Bioavailability of the drug and/or its metabolic profile
	Leachable and extractable profiles
User population	Whether product can be used safely and effectively

Step 2: What is missing for approval

Changes	Impacts
Drug constituent	Full characterization of drug
	Device delivery performance
User population	Whether product can be used safely and effectively

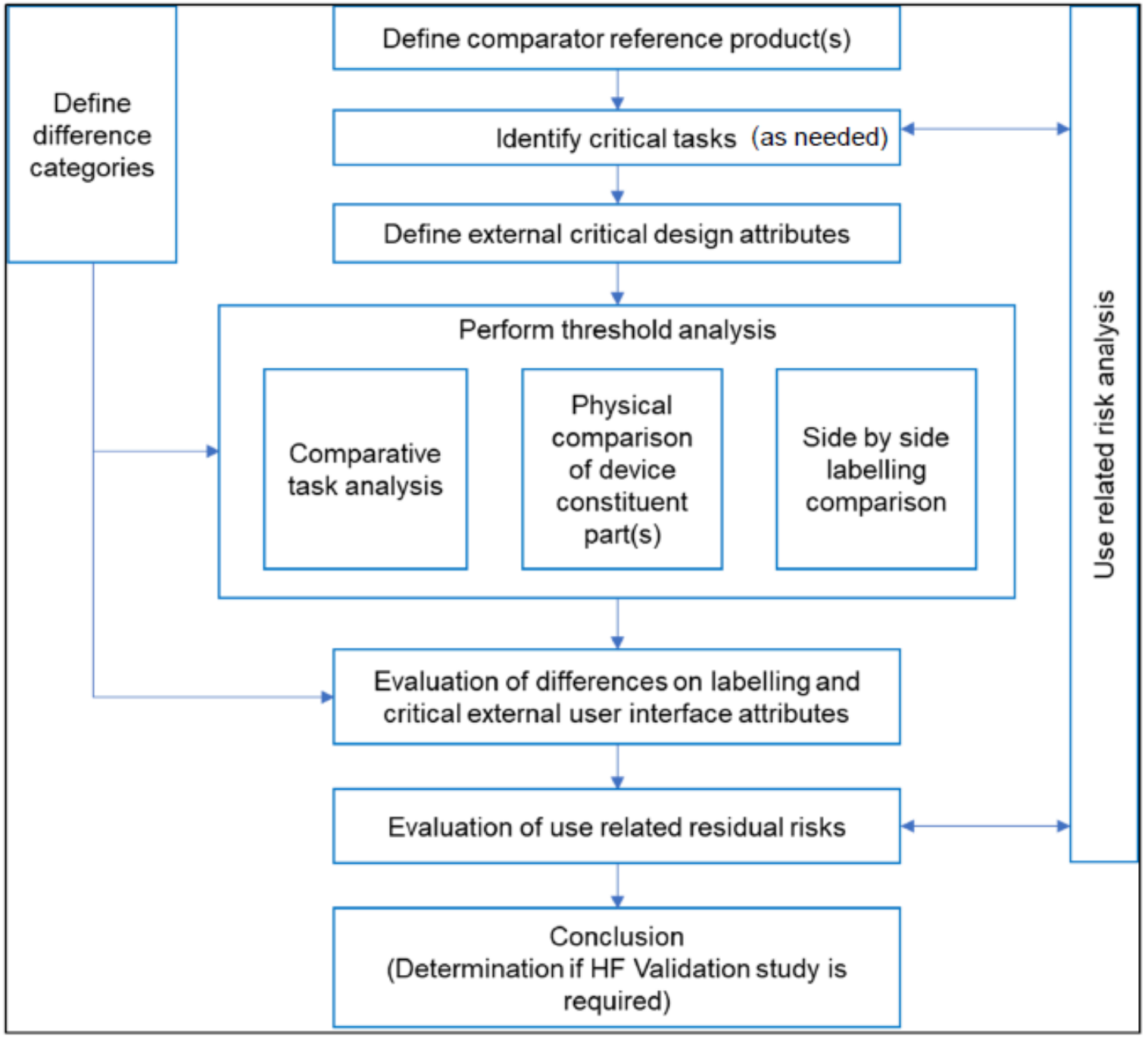
Step 3/4: What can be bridged and leveraged

- The drug agnostic tests (e.g. cap removal)
- Human Factors studies
- Biocompatibility

Step 5: What Gaps to address

- Reassess the applicability of the design inputs and outputs (design specs)
- Full scope of characterization on the drug side (compatibility, sterility)
- Clinical study
- Leachable/extractable
- Drug dependent tests (e.g. Dose accuracy; Break loose; extrusion force, CCI)

Overall Strategy



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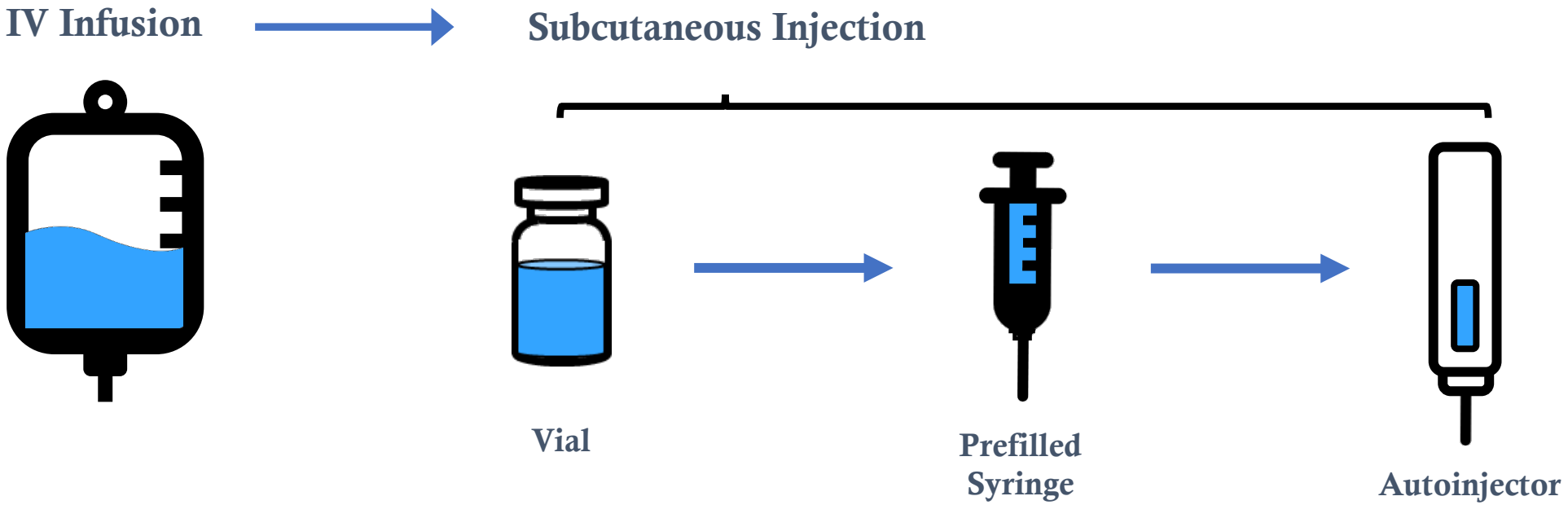
Combination Product Bridging Approach Examples Walkthrough

John McMichael, AstraZeneca

Nov. 2022

Bridging Walkthrough #1 – Parenteral Example

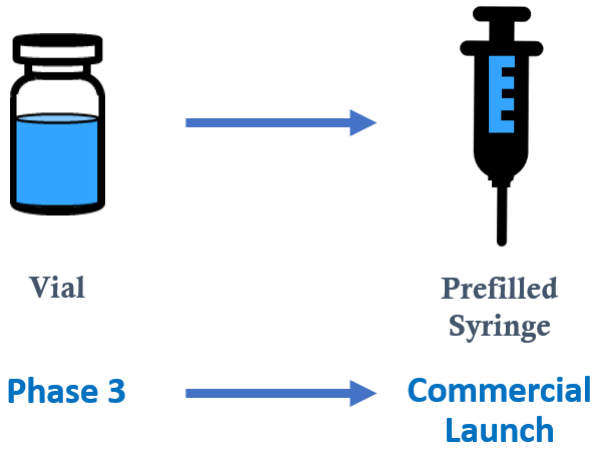


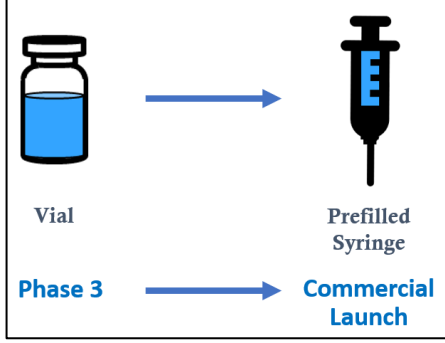
Vial to Pre-Filled Syringe

PharmaX aims to develop a single-dose pre-filled syringe for a biological product that has been studied in a vial in Phase 1 – 3 clinical studies. PharmaX plans to submit the pre-filled syringe for marketing authorization and commercial launch.

The pre-filled syringe is intended for HCP administration only, as was done for the vial injections conducted during Phase 3 clinical studies.

The formulation, concentration and dose volume will remain the same between clinical and commercial presentations. PharmaX has utilized the same syringe platform for multiple currently marketed products for different patient populations.





Bridging Approach

Step 1 Identify differences and impacts on safety and effectiveness

Step 2 Compare existing info of new device to approval requirements

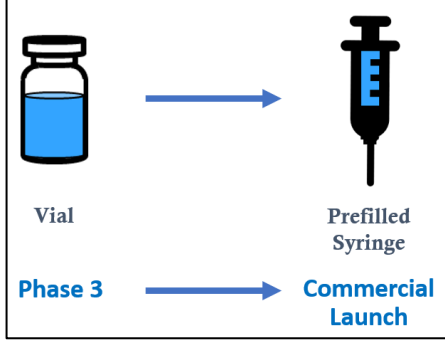
Step 3 Identify and leverage info on existing device

Step 4 Identify and leverage existing info on other products

Step 5 Fill remaining gaps

- New primary container closure
- New manufacturing process (e.g., assembly, packaging, fill-finish, etc.)
- Usability may be impacted

Bridging Approach



Step 1

Identify differences and impacts on safety and effectiveness

- New primary container closure
- New manufacturing process (e.g., assembly, packaging, fill-finish, etc.)
- Usability may be impacted

Step 2

Compare existing info of new device to approval requirements

- Full design controls package required for approval (e.g., design verification, design validation, risk management, etc.)
- PK comparability may be necessary between vial and PFS presentations to bridge to Ph3 S&E data

Step 3

Identify and leverage info on existing device

Step 4

Identify and leverage existing info on other products

Step 5

Fill remaining gaps

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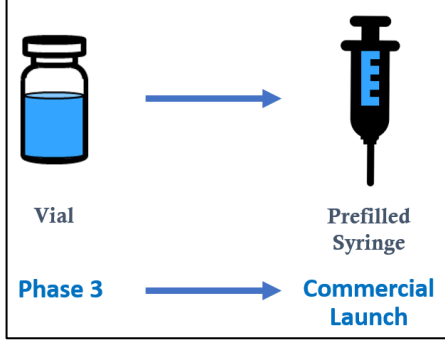
Bridging Approach



Step 1	Step 2	Step 3	Step 4	Step 5
Identify differences and impacts on safety and effectiveness	Compare existing info of new device to approval requirements	Identify and leverage info on existing device	Identify and leverage existing info on other products	Fill remaining gaps
• New primary container closure • New manufacturing process (e.g., assembly, packaging, fill-finish, etc.) • Usability may be impacted	• Full design controls package required for approval (e.g., design verification, design validation, risk management, etc.) • PK comparability may be necessary between vial and PFS presentations to bridge to Ph3 S&E data	• Any existing platform design verification data that is product-agnostic • Risk analysis information that is product-agnostic		

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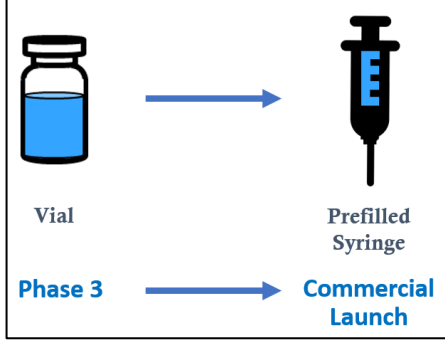
Bridging Approach



Step 1	Step 2	Step 3	Step 4	Step 5
Identify differences and impacts on safety and effectiveness	Compare existing info of new device to approval requirements	Identify and leverage info on existing device	Identify and leverage existing info on other products	Fill remaining gaps
• New primary container closure • New manufacturing process (e.g., assembly, packaging, fill-finish, etc.) • Usability may be impacted	• Full design controls package required for approval (e.g., design verification, design validation, risk management, etc.) • PK comparability may be necessary between vial and PFS presentations to bridge to Ph3 S&E data	• Any existing platform design verification data that is product-agnostic • Risk analysis information that is product-agnostic	• Any Human Factors data with similar user groups for other products	

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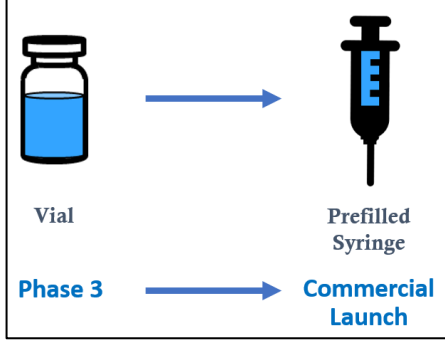
Bridging Approach



Step 1	Step 2	Step 3	Step 4	Step 5
Identify differences and impacts on safety and effectiveness	Compare existing info of new device to approval requirements	Identify and leverage info on existing device	Identify and leverage existing info on other products	Fill remaining gaps
• New primary container closure • New manufacturing process (e.g., assembly, packaging, fill-finish, etc.) • Usability may be impacted	• Full design controls package required for approval (e.g., design verification, design validation, risk management, etc.) • PK comparability may be necessary between vial and PFS presentations to bridge to Ph3 S&E data	• Any existing platform design verification data that is product-agnostic • Risk analysis information that is product-agnostic	• Any Human Factors data with similar user groups for other products	• Execute combo product design controls (e.g., design verification) • Conduct PK bridging study between vial and PFS • Determine if Human Factors Validation data necessary to support HCP-administration

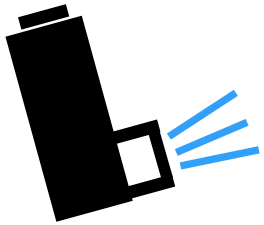
Bridging Walkthrough #2 – Inhalation Example

Nebulizer | Metered Dose Inhaler | Metered Dose Inhaler v2.0 | Metered Dose Inhaler v3.0

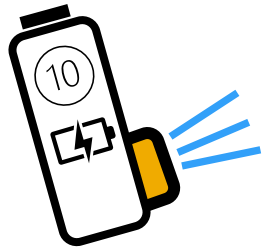
Phase 2 → **Phase 3** → **Commercial Launch** → **Post-Approval**

Pressurized Metered Dose Inhaler

CP Life has studied a pressurized metered dose inhaler (pMDI) throughout Phase 1 – 3 clinical studies. CP Life aims to add an integrated digital dose counter to the pMDI design prior to submission of marketing applications and commercial launch. The commercial device would also utilize a different color for the mouthpiece to align with the product branding. There are no changes to the formulation or dosage strength.



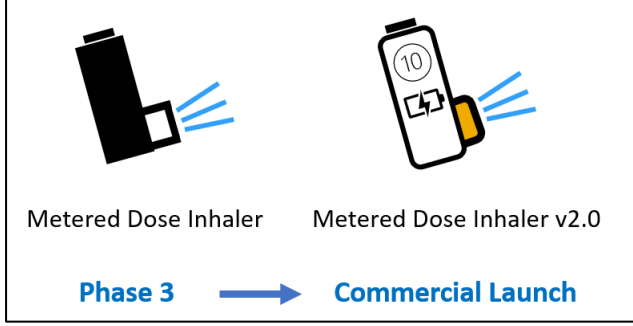
Metered Dose Inhaler



Metered Dose Inhaler v2.0

Phase 3 → **Commercial Launch**

Bridging Approach



Step 1: Identify differences and impacts on safety and effectiveness

Step 2: Compare existing info of new device to approval requirements

Step 3: Identify and leverage info on existing device

Step 4: Identify and leverage existing info on other products

Step 5: Fill remaining gaps

- Evaluate if any primary container / drug-contacting components are impacted by MDI changes
- Evaluate impact of electronics on drug product quality / stability
- Evaluate user interface differences and potential dosing errors

Bridging Approach

Metered Dose Inhaler | Metered Dose Inhaler v2.0

Phase 3 → Commercial Launch

Step 1 — Identify differences and impacts on safety and effectiveness

- Evaluate if any primary container / drug-contacting components are impacted by MDI changes
- Evaluate impact of electronics on drug product quality / stability
- Evaluate user interface differences and potential dosing errors

Step 2 — Compare existing info of new device to approval requirements

- Full design control package will be necessary to support approval of combination product
- If not yet developed for any other products, new data will need to be collected

Step 3 — Identify and leverage info on existing device

Step 4 — Identify and leverage existing info on other products

Step 5 — Fill remaining gaps

Bridging Approach

Metered Dose Inhaler | Metered Dose Inhaler v2.0

Phase 3 → Commercial Launch

Step 1	Step 2	Step 3	Step 4	Step 5
Identify differences and impacts on safety and effectiveness	Compare existing info of new device to approval requirements	Identify and leverage info on existing device	Identify and leverage existing info on other products	Fill remaining gaps

- Evaluate if any primary container / drug-contacting components are impacted by MDI changes
- Evaluate impact of electronics on drug product quality / stability
- Evaluate user interface differences and potential dosing errors

- Full design control package will be necessary to support approval of combination product
- If not yet developed for any other products, new data will need to be collected

- Determine if safety & efficacy data from Phase 3 study can be leveraged for new device by assessing comparability of product quality / dose delivery characteristics
- Determine is Leachables & Extractables can be leveraged

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Bridging Approach

Metered Dose Inhaler | Metered Dose Inhaler v2.0

Phase 3 → Commercial Launch

Step 1	Step 2	Step 3	Step 4	Step 5
Identify differences and impacts on safety and effectiveness	Compare existing info of new device to approval requirements	Identify and leverage info on existing device	Identify and leverage existing info on other products	Fill remaining gaps
• Evaluate if any primary container / drug-contacting components are impacted by MDI changes • Evaluate impact of electronics on drug product quality / stability • Evaluate user interface differences and potential dosing errors	• Full design control package will be necessary to support approval of combination product • If not yet developed for any other products, new data will need to be collected	• Determine if safety & efficacy data from Phase 3 study can be leveraged for new device by assessing comparability of product quality / dose delivery characteristics • Determine is Leachables & Extractables can be leveraged	• Evaluate if existing design verification data from Phase 3 device can be leveraged • Evaluate if in-vitro comparability can bridge to Phase 3 clinical data	

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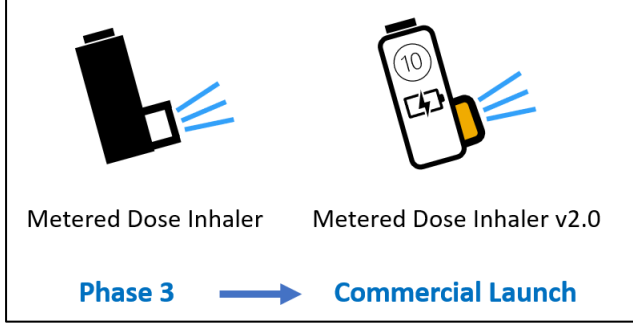
Bridging Approach



Step 1

Identify differences and impacts on safety and effectiveness

- Evaluate if any primary container / drug-contacting components are impacted by MDI changes
- Evaluate impact of electronics on drug product quality / stability
- Evaluate user interface differences and potential dosing errors

Step 2

Compare existing info of new device to approval requirements

- Full design control package will be necessary to support approval of combination product
- If not yet developed for any other products, new data will need to be collected

Step 3

Identify and leverage info on existing device

- Determine if safety & efficacy data from Phase 3 study can be leveraged for new device by assessing comparability of product quality / dose delivery characteristics
- Determine is Leachables & Extractables can be leveraged

Step 4

Identify and leverage existing info on other products

- Evaluate if existing design verification data from Phase 3 device can be leveraged
- Evaluate if in-vitro comparability can bridge to Phase 3 clinical data

Step 5

Fill remaining gaps

- Collect Human Factors Validation data on new user interface
- Collect design verification for new design requirements (e.g., firmware / electronics)
- Execute in-vitro comparability studies

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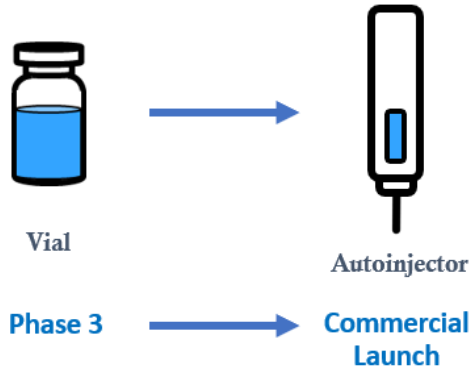
Tabletop Workshop Exercise

Exercise #1 - Autoinjector

BioZ aims to develop an autoinjector for a biological product that has been studied in a vial in Phase 1 – 3 clinical studies. The company plans to submit the autoinjector within the original marketing application for commercial launch alongside the vial presentation.

Phase 3 study injections were administered by HCPs in the clinic environment. The autoinjector is intended for self-administration at home.

The formulation, concentration and dose volume will remain the same between clinical and commercial presentations. BioZ has no prior experience with this autoinjector design.



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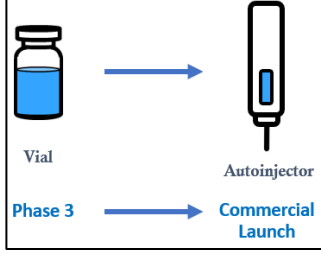
Exercise #1



Step 1	Step 2	Step 3	Step 4	Step 5
Identify differences and impacts on safety and effectiveness	**Compare existing info of new device to approval requirements**	**Identify and leverage info on existing device**	**Identify and leverage existing info on other products**	**Fill remaining gaps**
Identify all differences between the prior and new product presentation/process and consider the potential effect of differences on the safety and effectiveness profile.	Identify existing information that has been gathered or generated through studies and assessments for the prior product and compare it to the safety and effectiveness submission requirements necessary for approval of the new product.	Identify and explain how and why existing information for the prior product / process can be bridged and leveraged to support approval of the new product.	Focus on any information gaps remaining and consider whether other existing information can be reviewed and used to address these gaps.	Compare findings from Step 2 through 4 and identify the remaining gaps in information that need to be addressed for approval of the new product/

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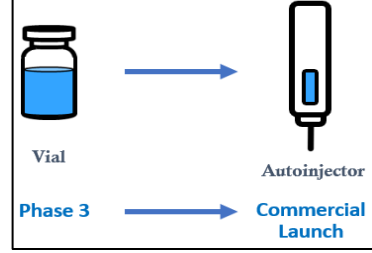
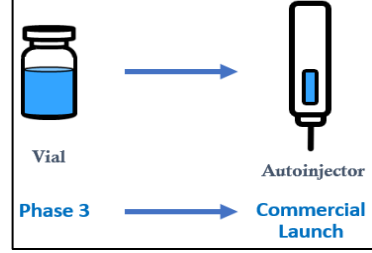


Step 1

Identify differences and impacts on safety and effectiveness

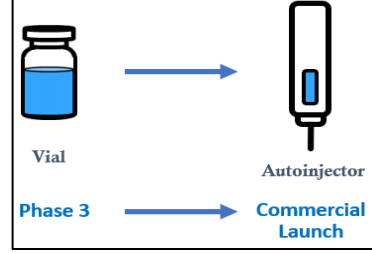
Identify all differences between the prior and new product presentation/process and consider the potential effect of differences on the safety and effectiveness profile.



Step 2

Compare existing info of new device to approval requirements

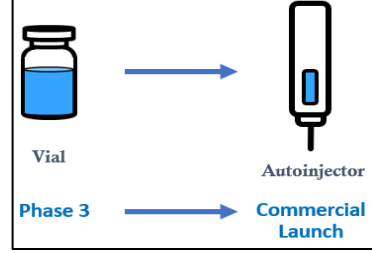
Identify existing information that has been gathered or generated through studies and assessments and compare it to the safety and effectiveness submission requirements necessary for approval.



Step 3

Identify and leverage info on existing device

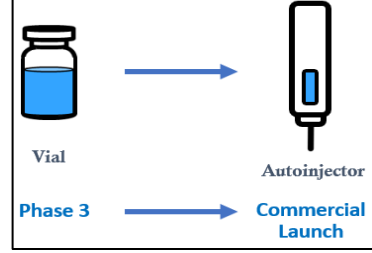
Identify and explain how and why existing information can be bridged and leveraged to support approval.



Step 4

Identify and leverage existing info on other products

Focus on any information gaps remaining from and consider whether other existing information can be reviewed and used to address these gaps.



Step 5

Fill remaining gaps

Compare findings from Step 2 through 4 and identify the remaining gaps in information that need to be addressed in the product application.

Exercise #2 – Multi-Dose Dry Powder Inhaler

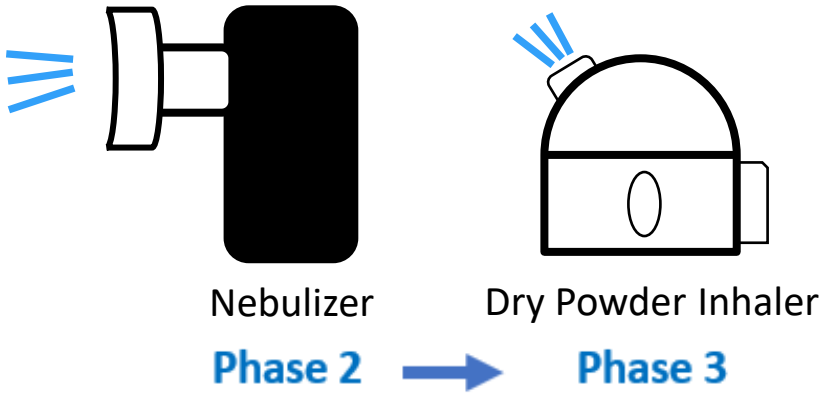
InhaleBio plans to develop a pre-filled multi-dose Dry Powder Inhaler (DPI) that contains a biological product to be self-administered for the treatment of Asthma.

InhaleBio studied the biological product in a nebulizer with loadable capsules during the clinical development program through Phase 2b clinical trials. The company plans to utilize the to-be-marketed multi-dose DPI during the pivotal Phase 3 clinical study to support a future marketing application for the product.

The product was administered by HCPs in Phase 2b trials and planned for self-administration at home for Phase 3 trials.

The results of the Phase 2b clinical study will be critical in supporting the commercial approval of the product, in addition to the upcoming Phase 3 studies.

The formulation and concentration will remain constant.



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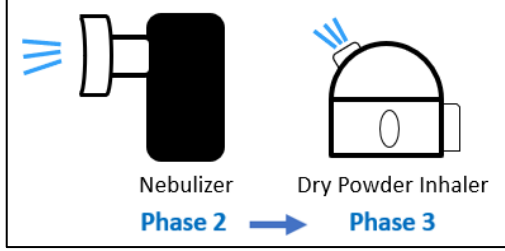
Exercise #2



Step 1	Step 2	Step 3	Step 4	Step 5
Identify differences and impacts on safety and effectiveness	**Compare existing info of new device to approval requirements**	**Identify and leverage info on existing device**	**Identify and leverage existing info on other products**	**Fill remaining gaps**
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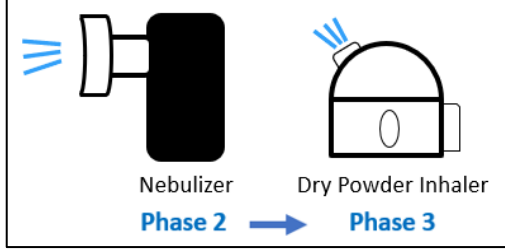
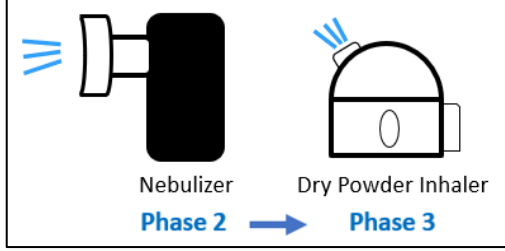


Step 1

Identify differences and impacts on safety and effectiveness

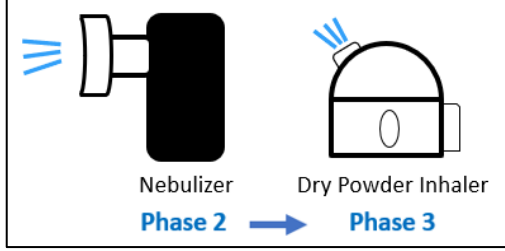
Identify all differences between the prior and new product presentation/process and consider the potential effect of differences on the safety and effectiveness profile.



Step 2

Compare existing info of new device to approval requirements

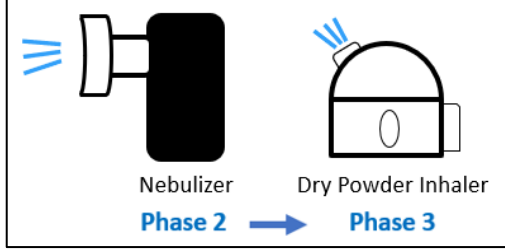
Identify existing information that has been gathered or generated through studies and assessments and compare it to the safety and effectiveness submission requirements necessary for approval.



Step 3

Identify and leverage info on existing device

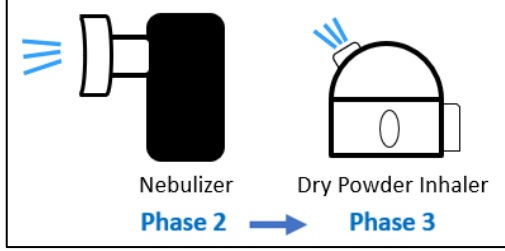
Identify and explain how and why existing information can be bridged and leveraged to support approval.



Step 4

Identify and leverage existing info on other products

Focus on any information gaps remaining from and consider whether other existing information can be reviewed and used to address these gaps.



Step 5

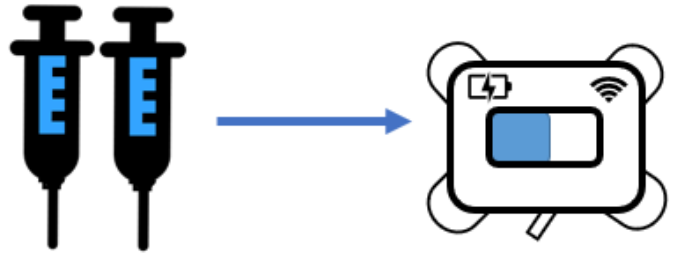
Fill remaining gaps

Compare findings from Step 2 through 4 and identify the remaining gaps in information that need to be addressed in the product application.

Exercise #3 – On Body Injector

OBDZ plans to develop an electromechanical on-body injector as an additional drug delivery system for their biological product that is currently marketed in the form of multiple pre-filled syringe injections (total dose volume ~8mL). The formulation and concentration will remain unchanged.

OBDZ utilized their currently marketed 2 mL pre-filled syringes during Phase 3 clinical studies and has no clinical experience with the novel on-body injection system. The device is intended to be worn by patients at home for approximately 15 minutes and the injection progress can be monitored in real-time by users on a custom-made smartphone mobile application via Bluetooth connection with the injector.



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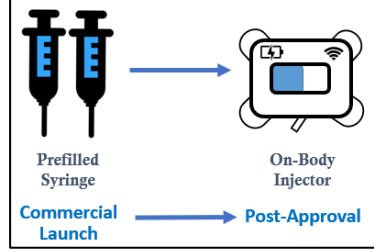
Exercise #3



Step 1	Step 2	Step 3	Step 4	Step 5
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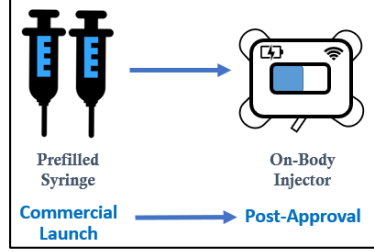

Step 1

Identify differences and impacts on safety and effectiveness

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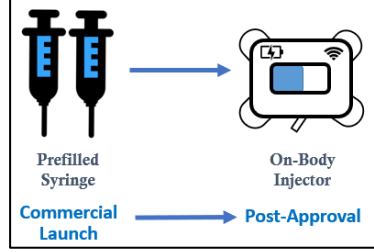
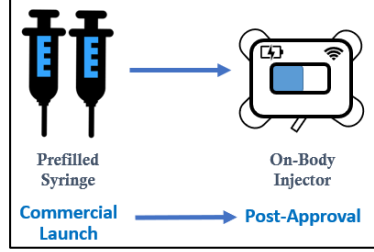


Step 2

Compare existing info of new device to approval requirements

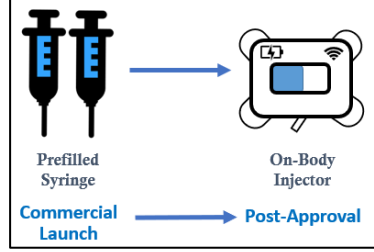
Identify existing information that has been gathered or generated through studies and assessments and compare it to the safety and effectiveness submission requirements necessary for approval.



Step 3

Identify and leverage info on existing device

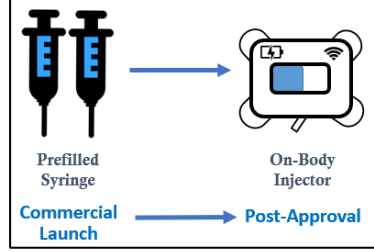
Identify and explain how and why existing information can be bridged and leveraged to support approval.



Step 4

Identify and leverage existing info on other products

Focus on any information gaps remaining from and consider whether other existing information can be reviewed and used to address these gaps.



Step 5

Fill remaining gaps

Compare findings from Step 2 through 4 and identify the remaining gaps in information that need to be addressed in the product application.