

WEBINAR – June 25, 2009

Shoot for Share! From Vial to Pre-filled Syringe

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Baxter BioPharma Solutions

Today we will address:

- Why?** Value proposition of moving to a pre-filled syringe
- What?** Regulatory plan to enable move
- How?** Process to move from vial (liquid or lyophilized) to syringe
- Who?** CMO qualifications

WHY?

VALUE PROPOSITION

Why?

Market driven

Line extension – Life cycle management

- New presentation
- New administration route

Latest Technology / Market edge

- Competition
- Pharmacoeconomics

Customer driven

Safety- fewer manipulations

Accuracy- Dose delivered

Quality of life- self administered

Product driven

Manufacturing

Less API waste → increased units filled → increased revenue

Why? - Strategies to Improve the Value of a Biologic Molecule

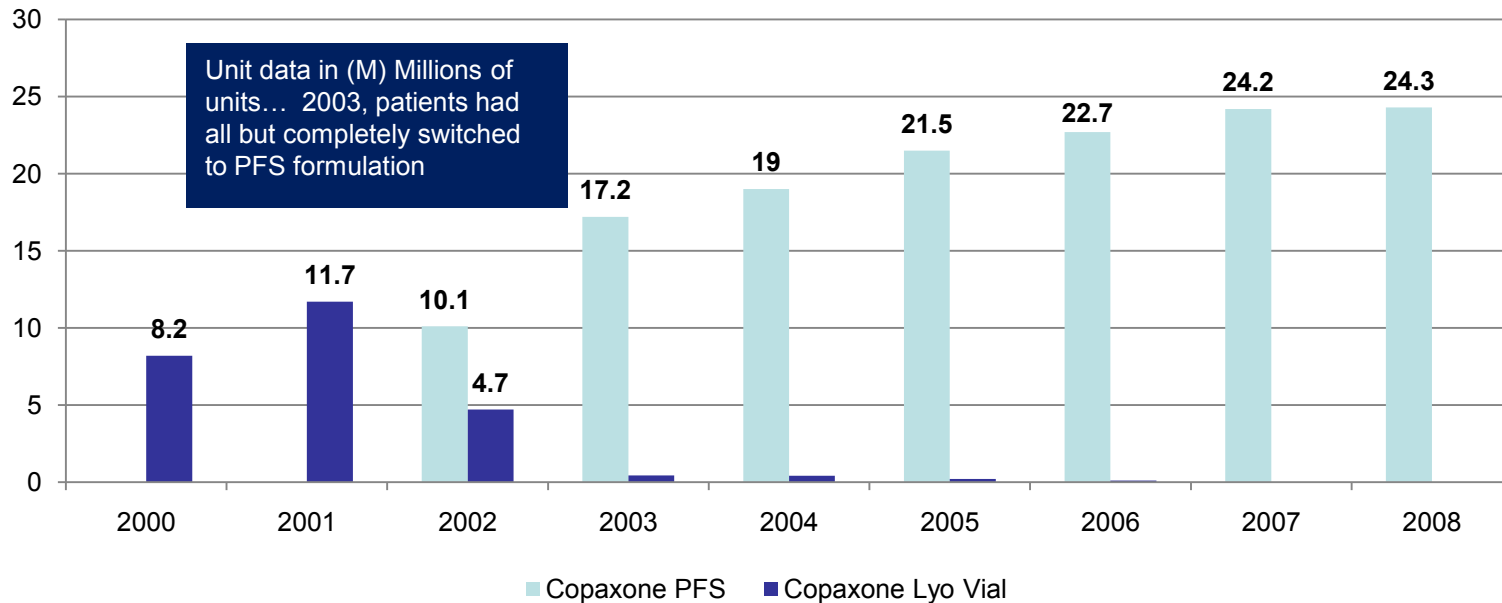
Due to the inherent challenges of biologics, enhancements are difficult yet the market rewards improvements

Short-Term Strategy (6-18 Months)	Mid-Term Strategy (18-36 Months)	Long-Term Strategy (>36 Months)
Attach a safety device to a pre-filled syringe Kit vials with a ready to use diluent syringe Move from a stable liquid vial to a pre-filled syringe	Move from a vial or syringe into an autoinjector or cartridge Reformulate lyophilized vials into a liquid vial or pre-filled syringe	Develop sustained release formulation Develop alternate route formulation

Short and Mid -Term strategies can help to differentiate a biologic molecule

Why? - Mid-Term Strategy

Teva Pharmaceutical Industries Ltd changes the presentation of Copaxone® from a dry vial preparation to a pre-filled syringe.

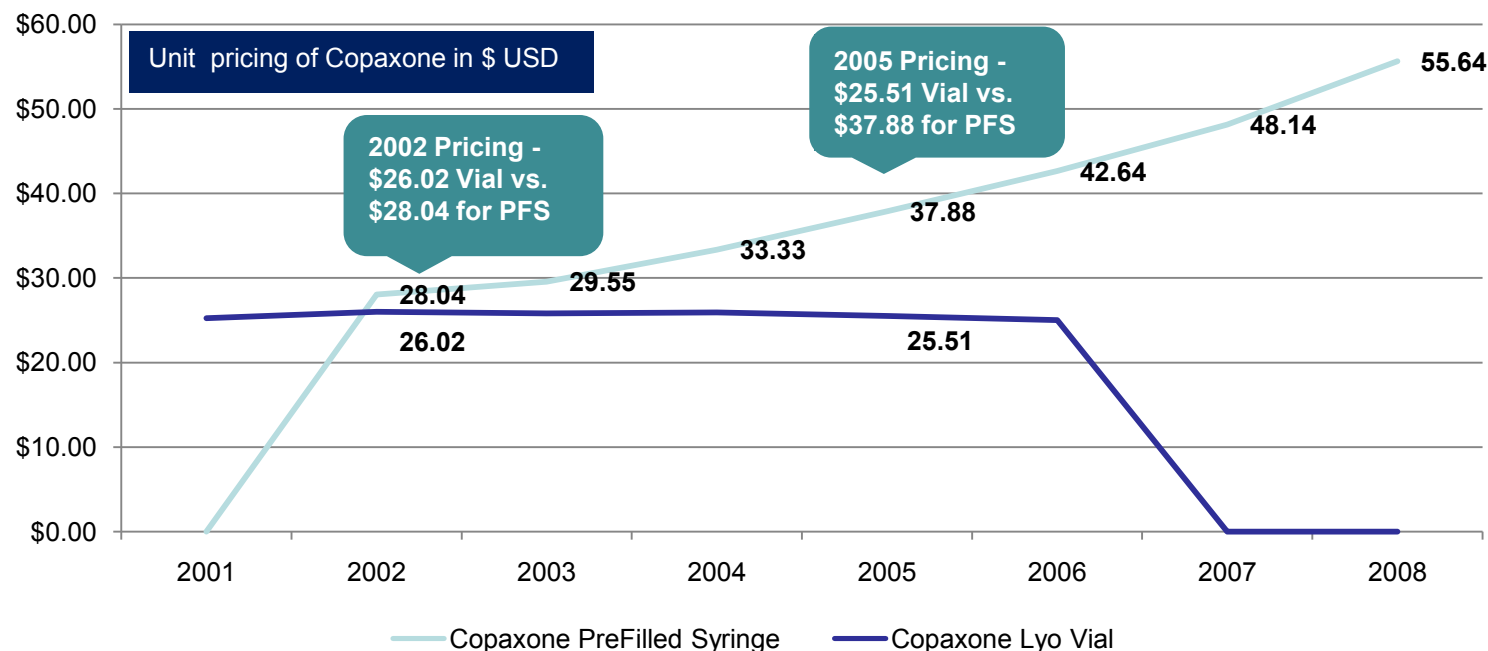


Copaxone PFS achieved rapid uptake in the US, with 64% of patients switching within the first three months from the dry vial formulation to the new formulation, and the remainder had switched within six months of launch.

Dry vial to Syringe – rapid uptake 64% switched in 3 months, remainder in 6 months after launch

Why? - Mid-Term Strategy

The Copaxone[®] reformulation was priced at a premium as compared to the original formulation. In 2002 the premium started at 5%, however, by 2005 the price premium was 48.6%.



For patients, the switch reduced average preparation time from 235 seconds (reconstituted Copaxone) to 38 seconds, saving more than 20 hours over the course of a year.

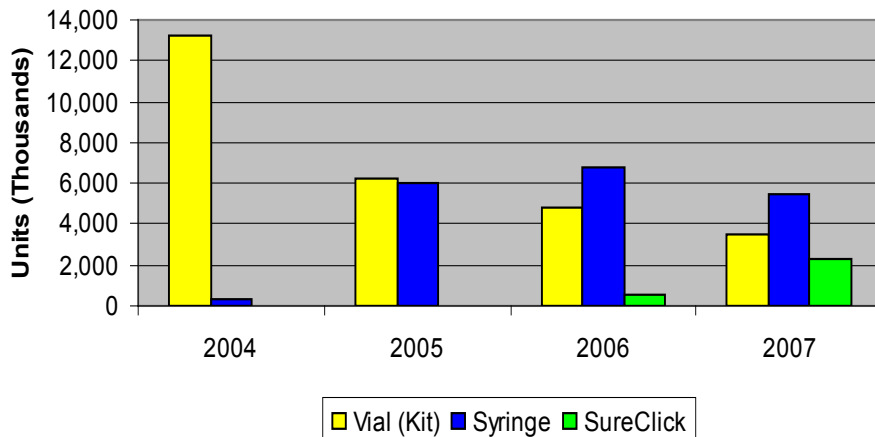
Premium pricing - from 5% in 2002 to 49% by 2005.

Preparation time reduced from 4 minutes to 38 seconds.

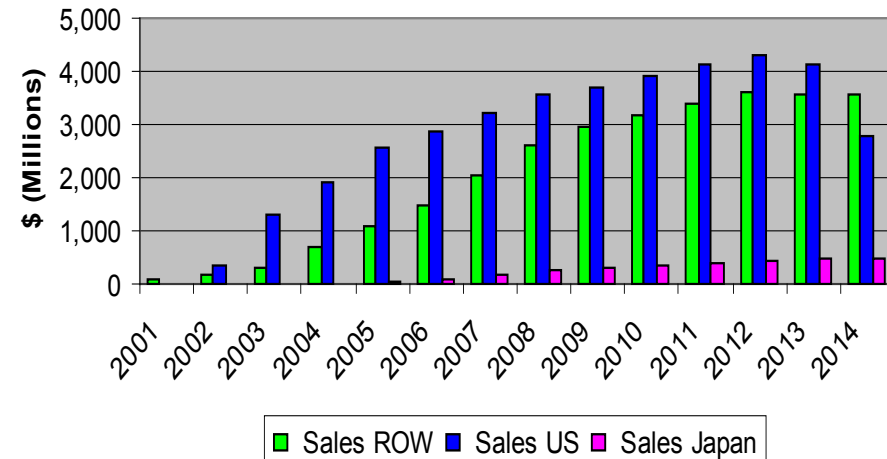
Why? - Mid-Term Strategy

Amgen, Inc. changed the presentation of Enbrel from a dry vial preparation to a pre-filled syringe. To further differentiate and add value, in 2006 Enbrel launched in an auto injector.

Enbrel Presentation Mix



Enbrel WW Sales



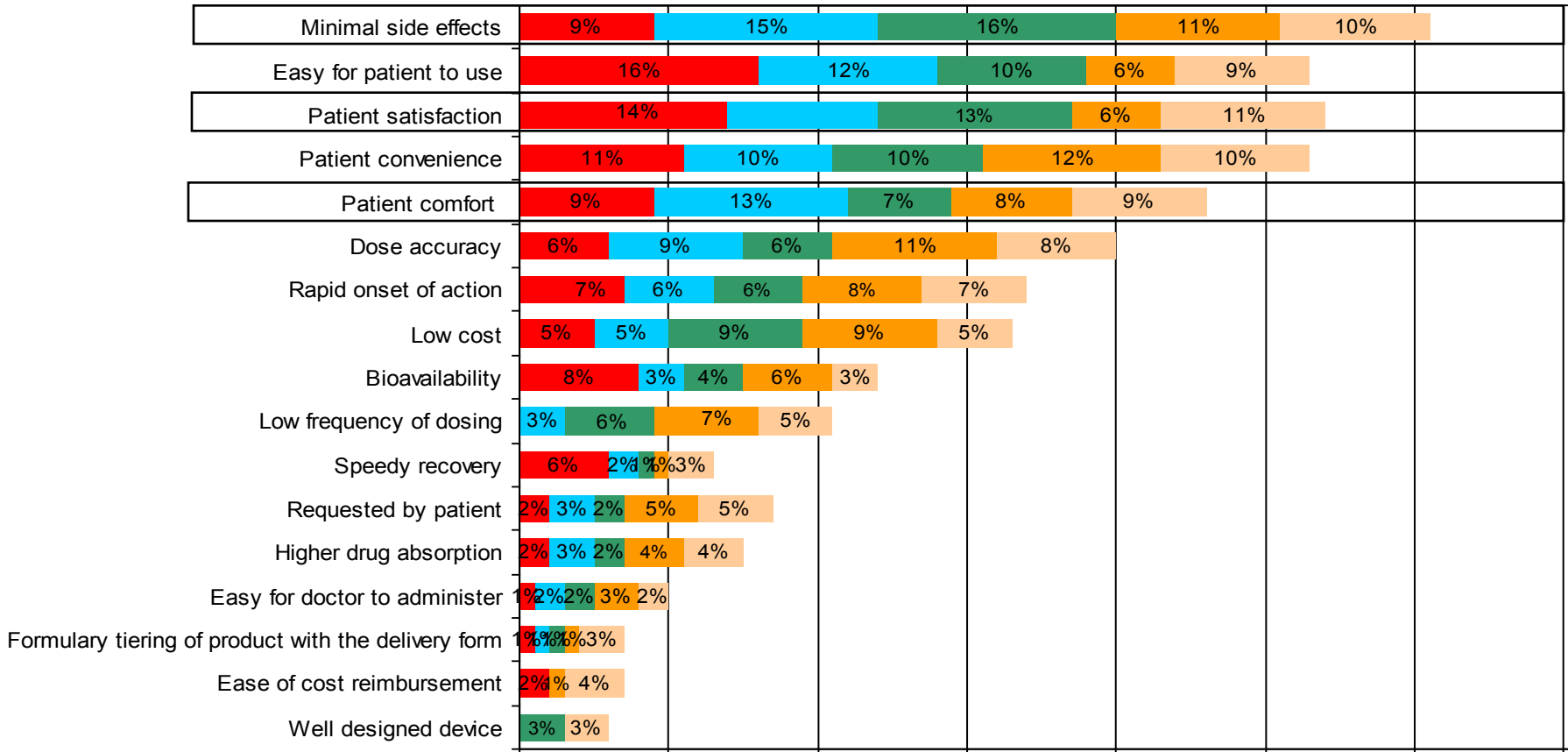
Overall Enbrel unit sales have remained stable, however revenue has increased due to the price premium the PFS and SureClick™ format.

Revenue increased due to price premium; unit sales stable

Why? - Selecting a Drug Delivery Type



Doctors' top factors : minimal side effects, patients ease of use, satisfaction, convenience, comfort. Three of five factors (underlined) impacted by product presentation.

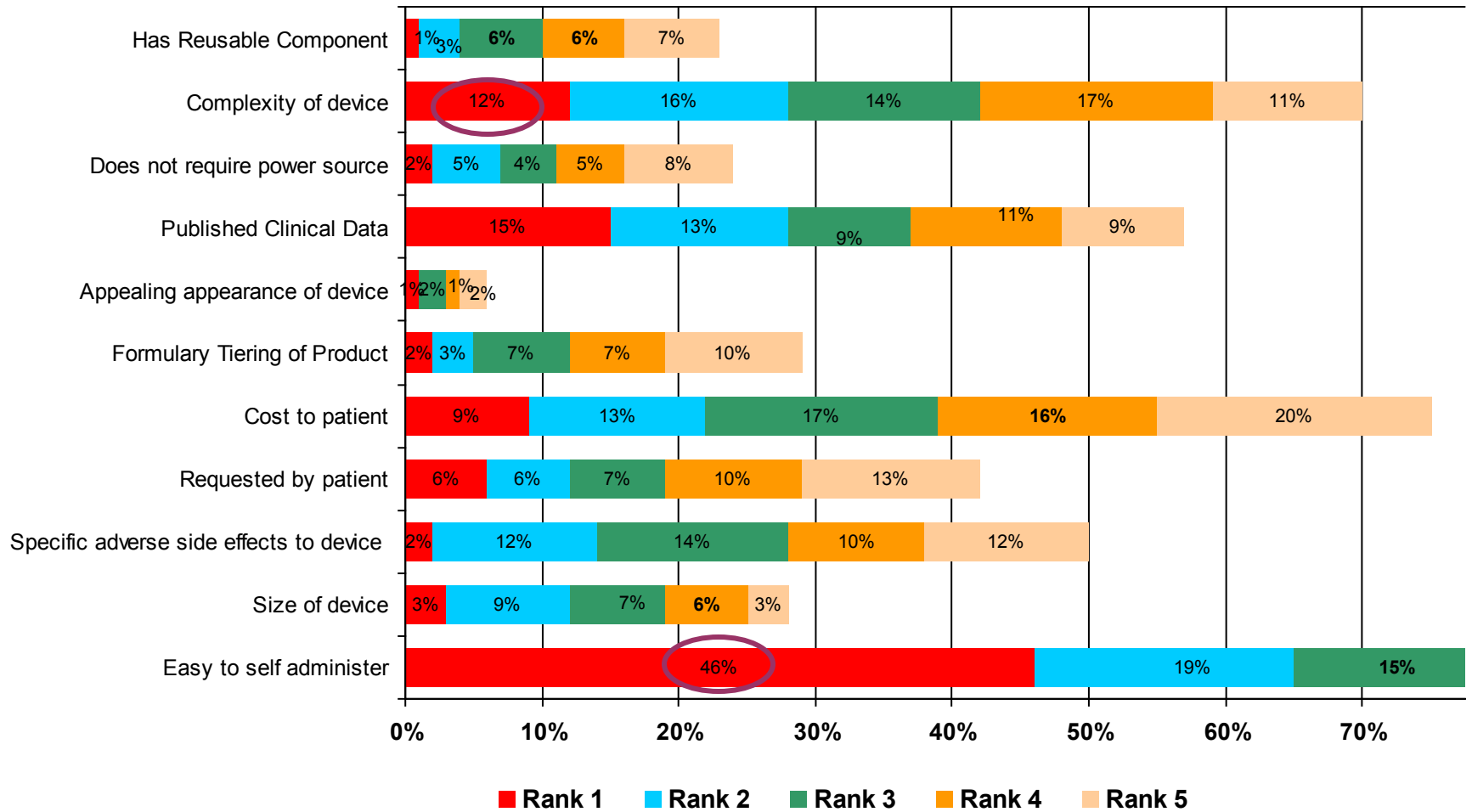


Question:

In order of importance, please select the top 5 factors that you consider when selecting a drug delivery type? (1= most important, 2=2nd most important, 3=3rd most important, etc.)

Why? Selecting Drug Delivery Type - Physician *Baxter*

Ease of self administering is the top reason for selecting a device type.

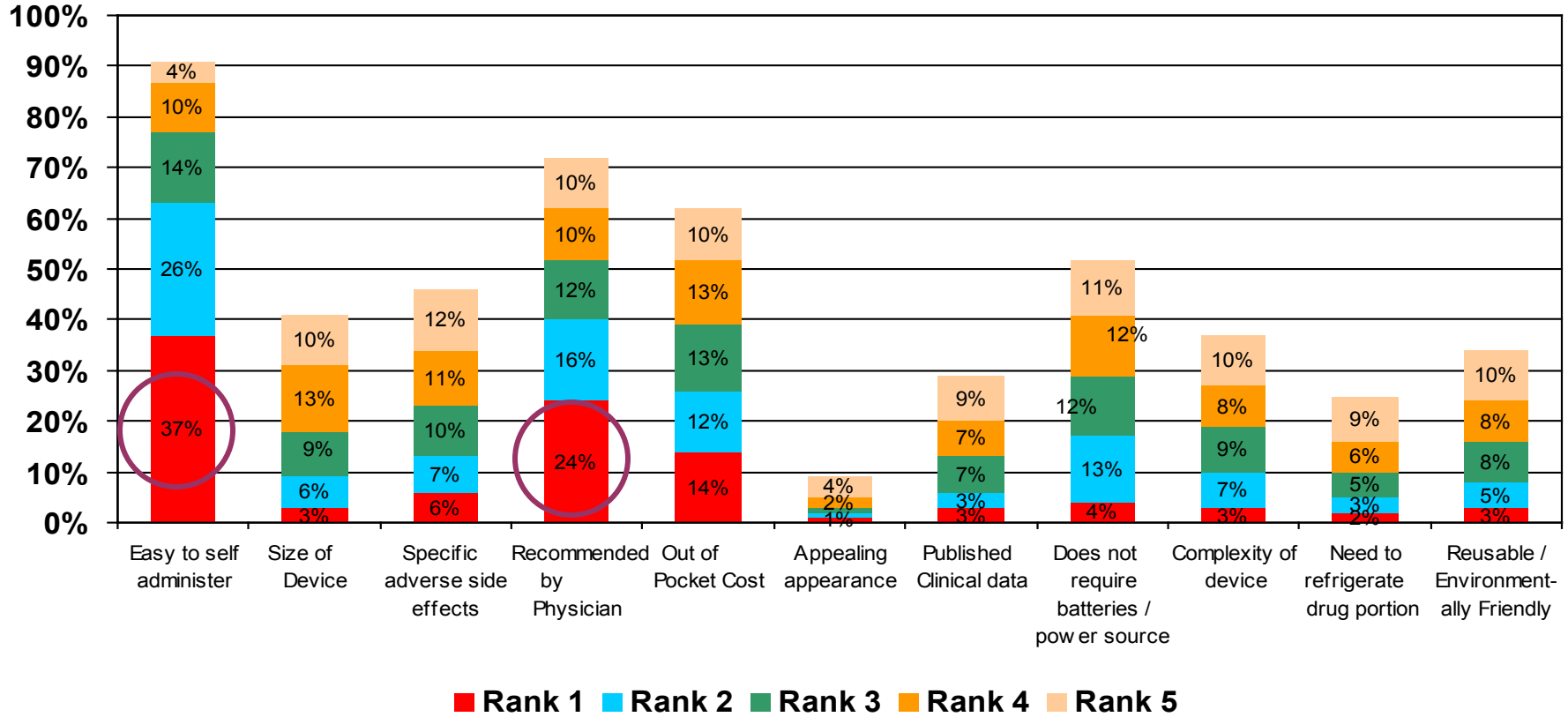


Question:
For Device Driven Drug Delivery (Examples: Inhaler, Autoinjector), please select the top 5 factors that most influence your decision to prescribe the product to your patients?

Why? Device Drug Delivery Method - Patient



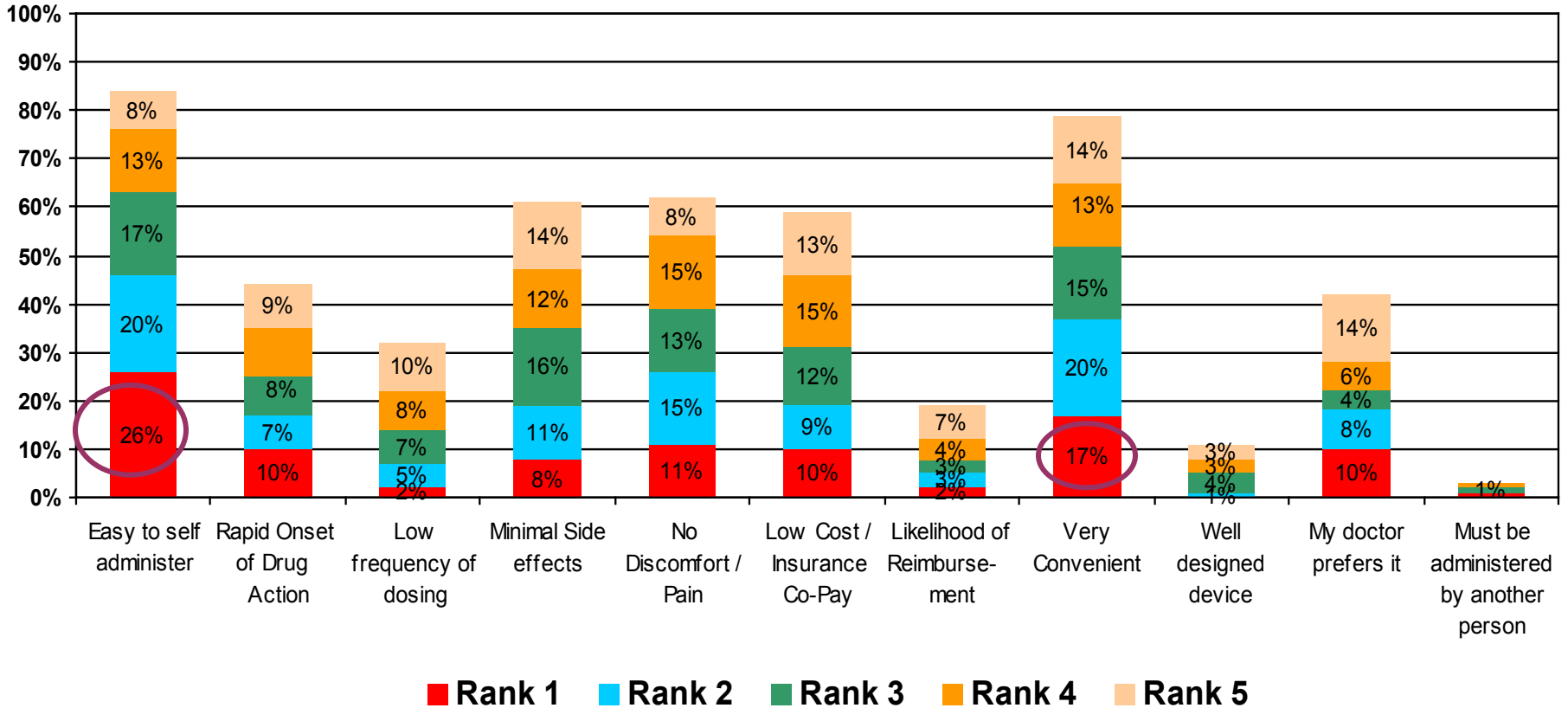
Top Factors are ease of self administration (37%) followed by Physician's recommendation (24%)



Question:
 For Device Driven Drug Delivery what are the top 5 factors that you consider? (1=most important, 2=2nd most important, 3=3rd most important, etc.)

Why? Device Drug Delivery Method – Patient *Baxter*

Ease of self administering is the most important factor for selecting drug delivery type followed by convenience.



Question:
 In order of importance, please select the top 5 factors that you consider when selecting a drug delivery type? (1= most important, 2=2nd most important, 3=3rd most important, etc.)

WHAT?

REGULATORY STRATEGY

What?

Define Regulatory Strategy

Regulatory considerations – Major change to regulatory market approval . . . Manageable

What?

Define Regulatory Strategy		
Evaluate & compare the proposed syringe system to approved materials		
<ul style="list-style-type: none"> ✓ Protects the drug product? ✓ Introduce a new material? ✓ Need drug product formulation changes? 		

Regulatory considerations – Major change to regulatory market approval . . . Manageable

What?

Define Regulatory Strategy		
Evaluate & compare the proposed syringe system to approved materials	Need supporting clinical data?	
<ul style="list-style-type: none"> ✓ Protects the drug product? ✓ Introduce a new material? ✓ Need drug product formulation changes? 	<ul style="list-style-type: none"> ✓ Safety or efficacy effect? ✓ New indication? ✓ New route of administration? 	

Regulatory considerations – Major change to regulatory market approval . . . Manageable

What?

Define Regulatory Strategy		
Evaluate & compare the proposed syringe system to approved materials	Need supporting clinical data?	Perform Stability protocol - New Dosage Form
<ul style="list-style-type: none"> ✓ Protects the drug product? ✓ Introduce a new material? ✓ Need drug product formulation changes? 	<ul style="list-style-type: none"> ✓ Safety or efficacy effect? ✓ New indication? ✓ New route of administration? 	<ul style="list-style-type: none"> ✓ Define stability requirements ✓ Execute stability protocol ✓ Analyze stability data

Regulatory considerations – Major change to regulatory market approval . . . Manageable

HOW?

VIAL TO SYRINGE

How?

REGULATORY STRATEGY

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graph TD; A[REGULATORY STRATEGY] --- B[Formulation Study]; A --- C[Stability Study]; A --- D[Clinical Study]; A --- E[Filing]; B --> C; C --> D; D --> E;
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**Formulation
Study**

**Stability
Study**

**Clinical
Study**

Filing

How?

REGULATORY STRATEGY

Formulation Study

Stability Study

Clinical Study

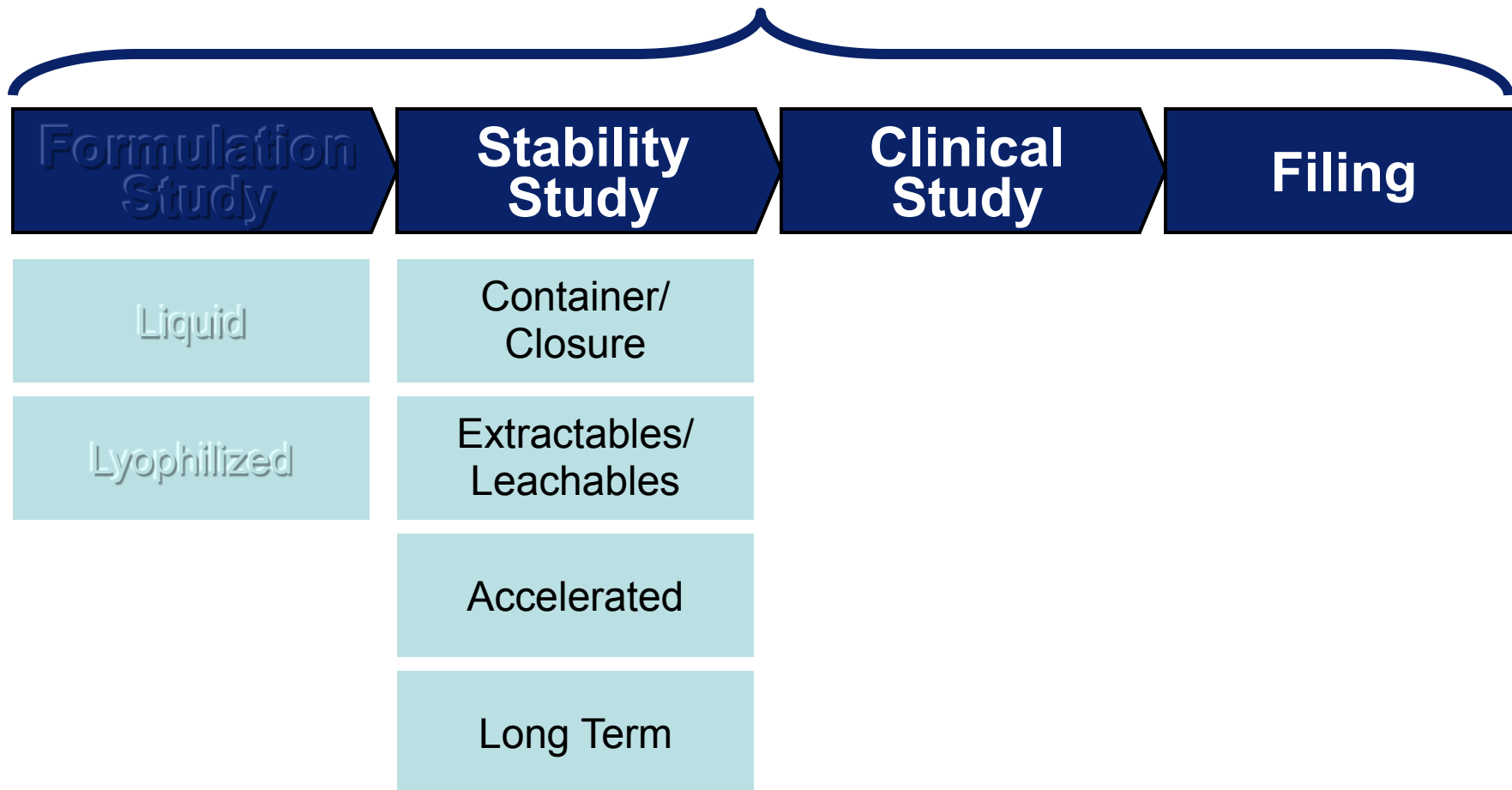
Filing

Liquid

Lyophilized

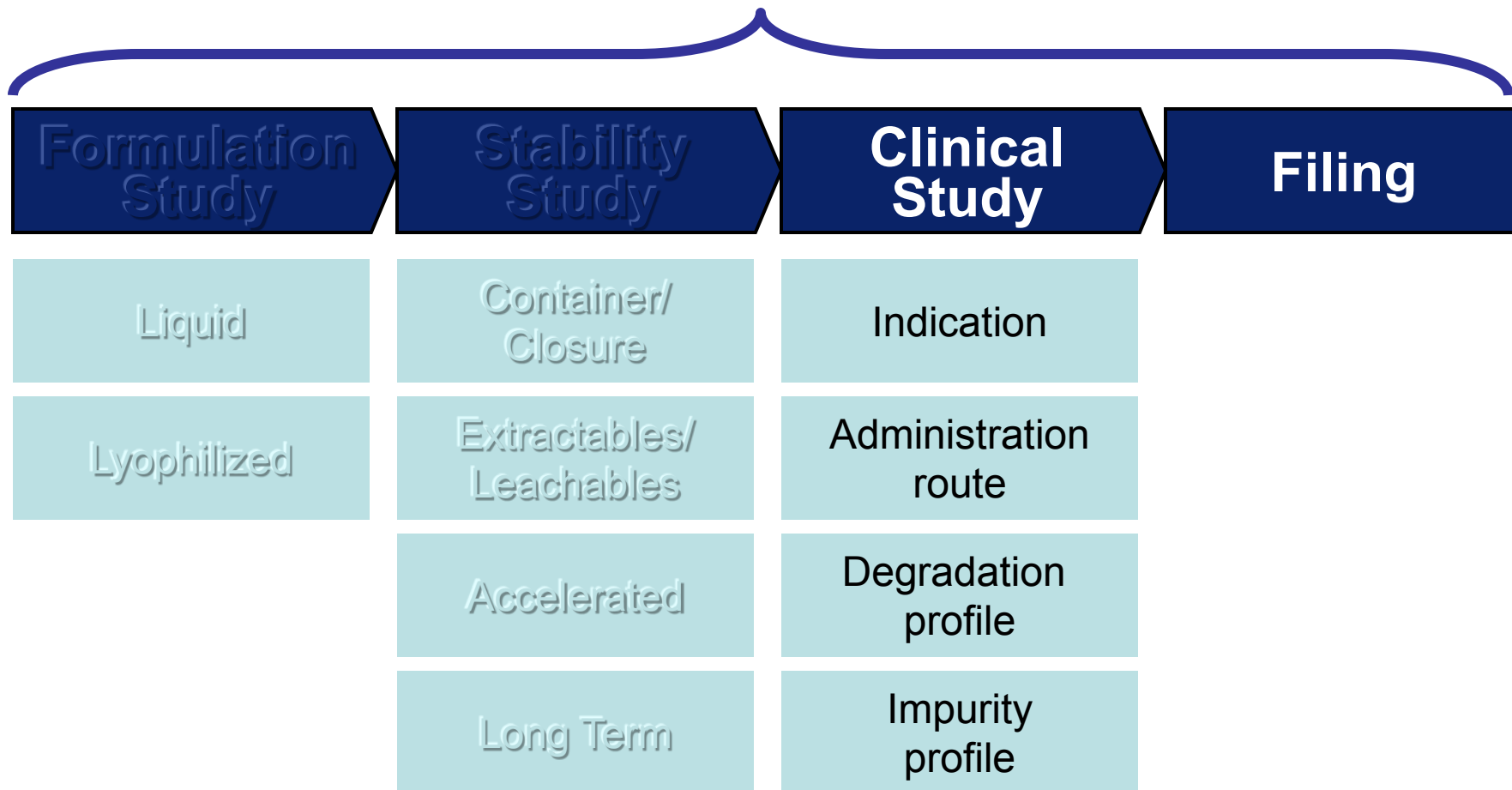
How?

REGULATORY STRATEGY



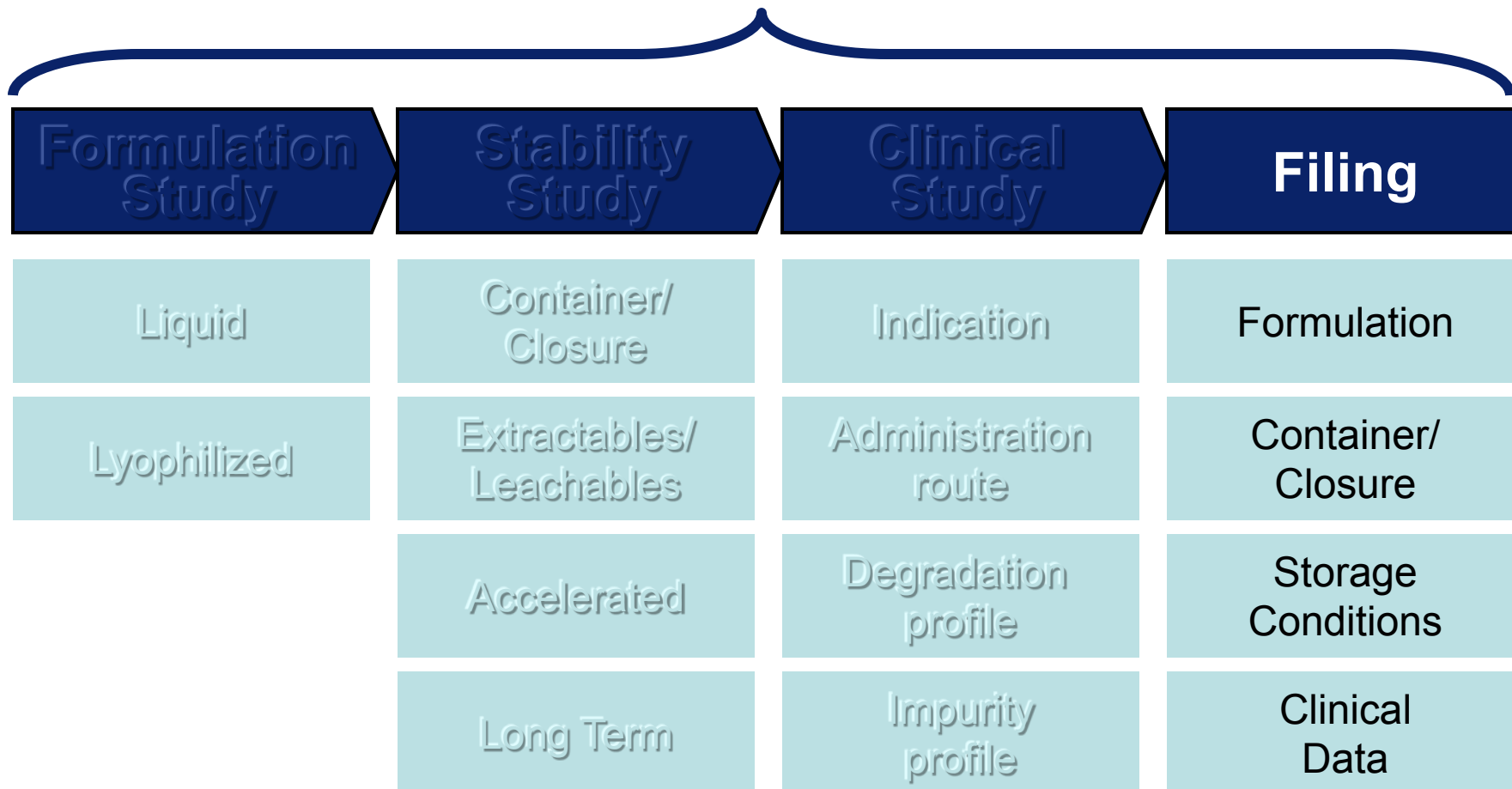
How?

REGULATORY STRATEGY



How?

REGULATORY STRATEGY



How?

Pre-filled syringe filing details:

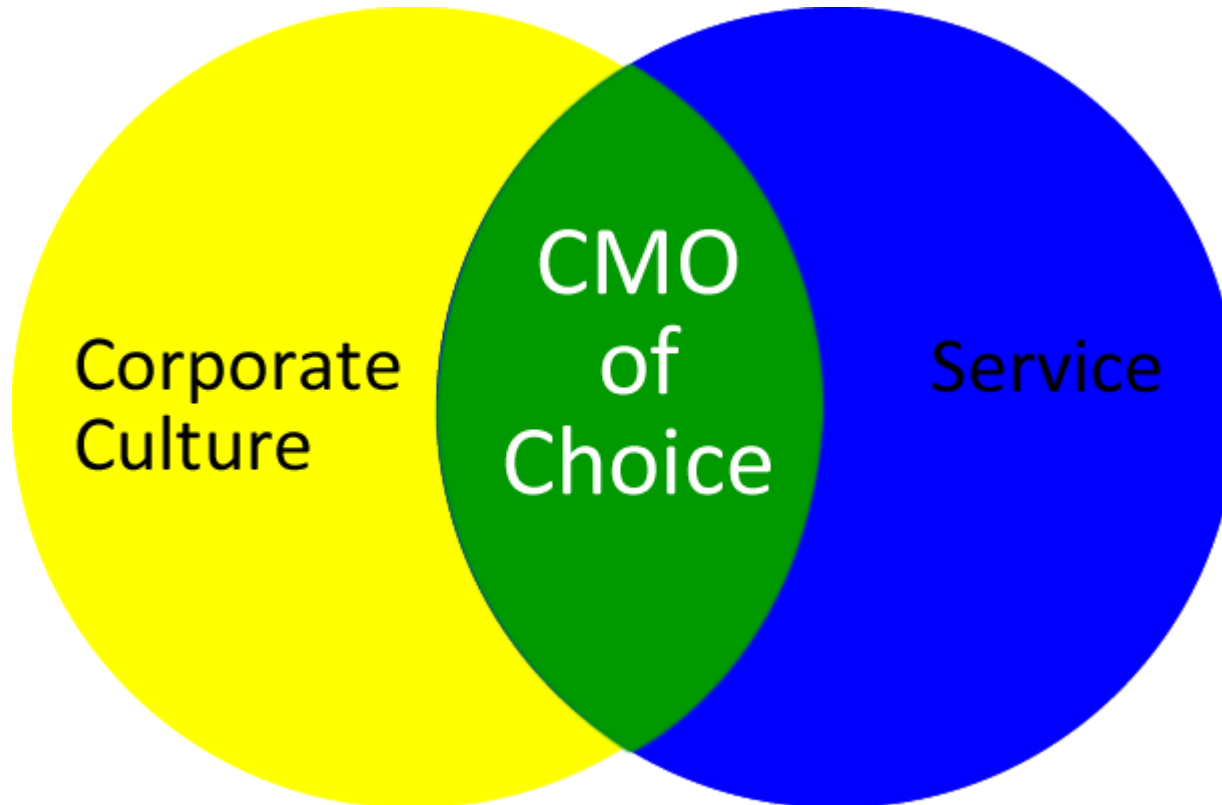
Attribute*	Move From Liquid Vial	Move From Lyo Vial
Container/Closure	Similar? Leverage previous extractable/leachable studies. Functionality: siliconization may be needed.	
Formulation	No change.	Change from freeze-dried powder to liquid.
Storage Conditions	No change. <u>Stability Study</u> : 3 months comparative accelerated and long term of at least 1 batch (3 may be required). <u>Clinical Study</u> : If degradation profile or impurities profile change.	May change <u>Stability Study</u> : 3 months comparative accelerated and long term data on 3 batches. <u>Clinical Study</u> : If degradation profile or impurities profile change.

* Indication and Administration Route changes need clinical data

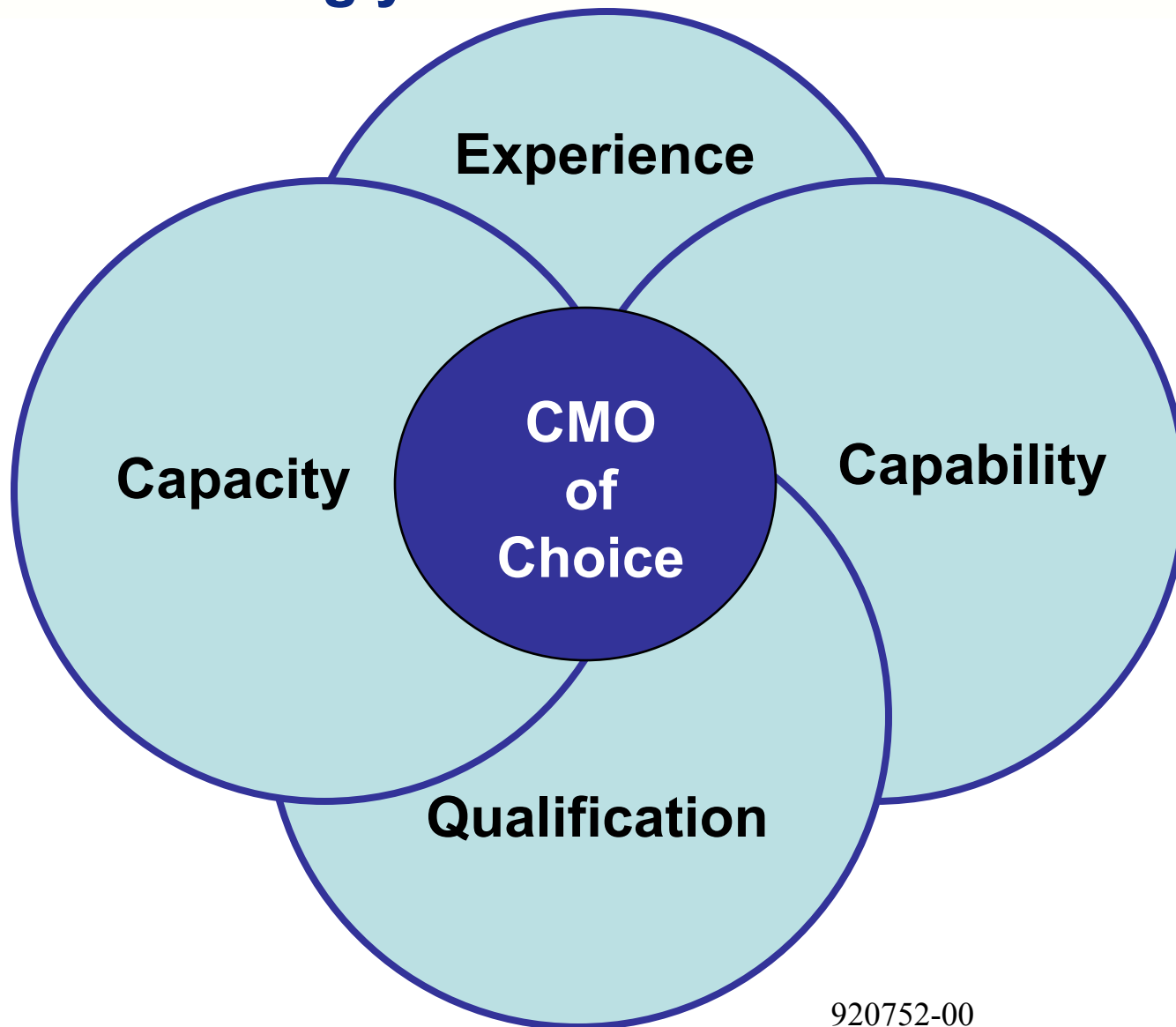
WHO?

CMO REQUIREMENTS

Who?



Who? Choosing your CMO . . .



Experience

Regulatory

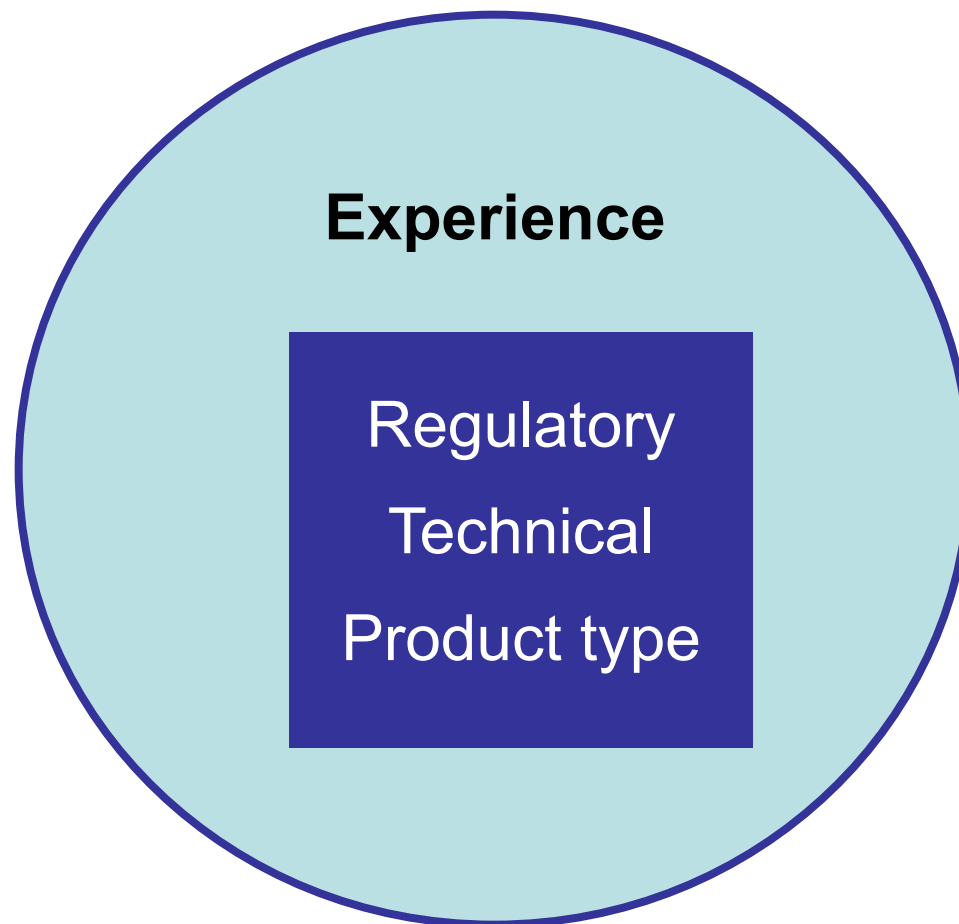
- ✓ Global and local compliance
- ✓ Audit history
- ✓ Regulatory review and approval process

Technical

- ✓ Product Scope
- ✓ Seasonal Campaign
- ✓ Market/Industry Presence

Product Type

- ✓ Small Molecules
- ✓ Biologicals



Capability

Resources

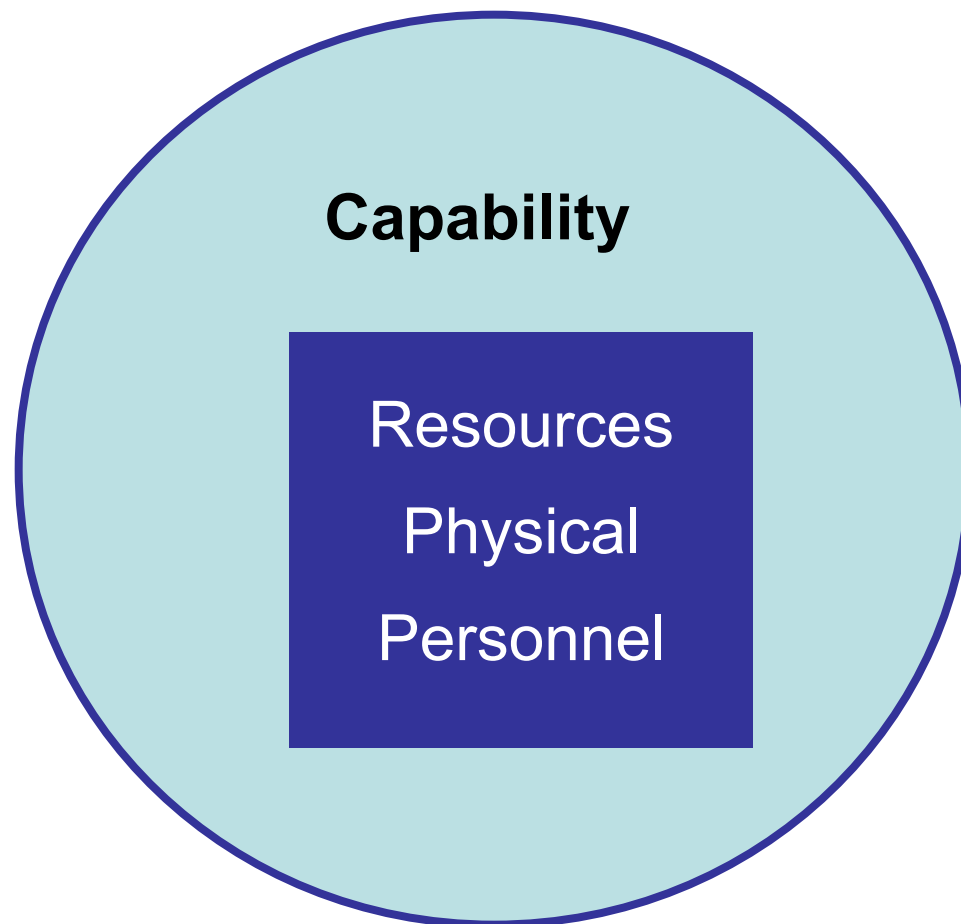
- ✓ Part of global company
- ✓ Redundancy
- ✓ Multidisciplinary

Physical

- ✓ Facility
- ✓ Aseptic Formulation
- ✓ Cold Chain Management

Personnel

- ✓ Education
- ✓ Training
- ✓ Experience



Qualification

Good Manufacturing Practices

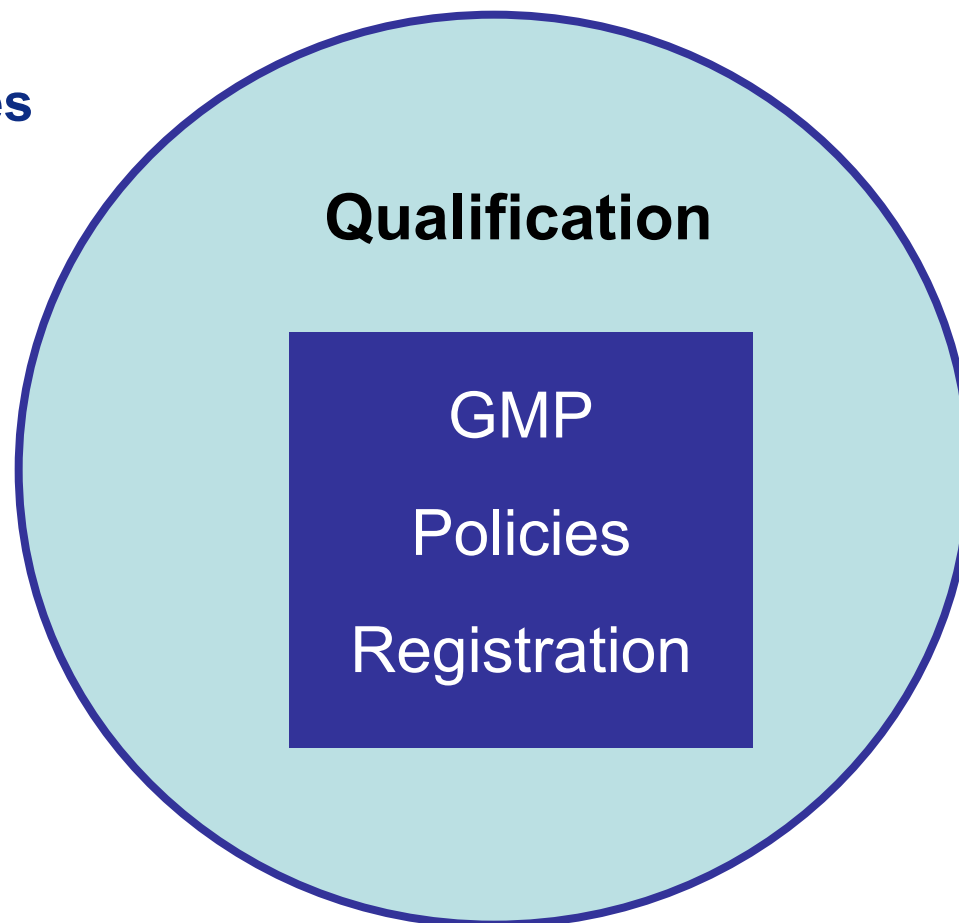
- ✓ Compliance
- ✓ Documentation
- ✓ Training
- ✓ Audit

Company Policies

- ✓ Business
- ✓ Quality
- ✓ Regulatory
- ✓ Manufacturing

Registration

- ✓ National entities
- ✓ Regulatory Agencies



Capacity

Equipment

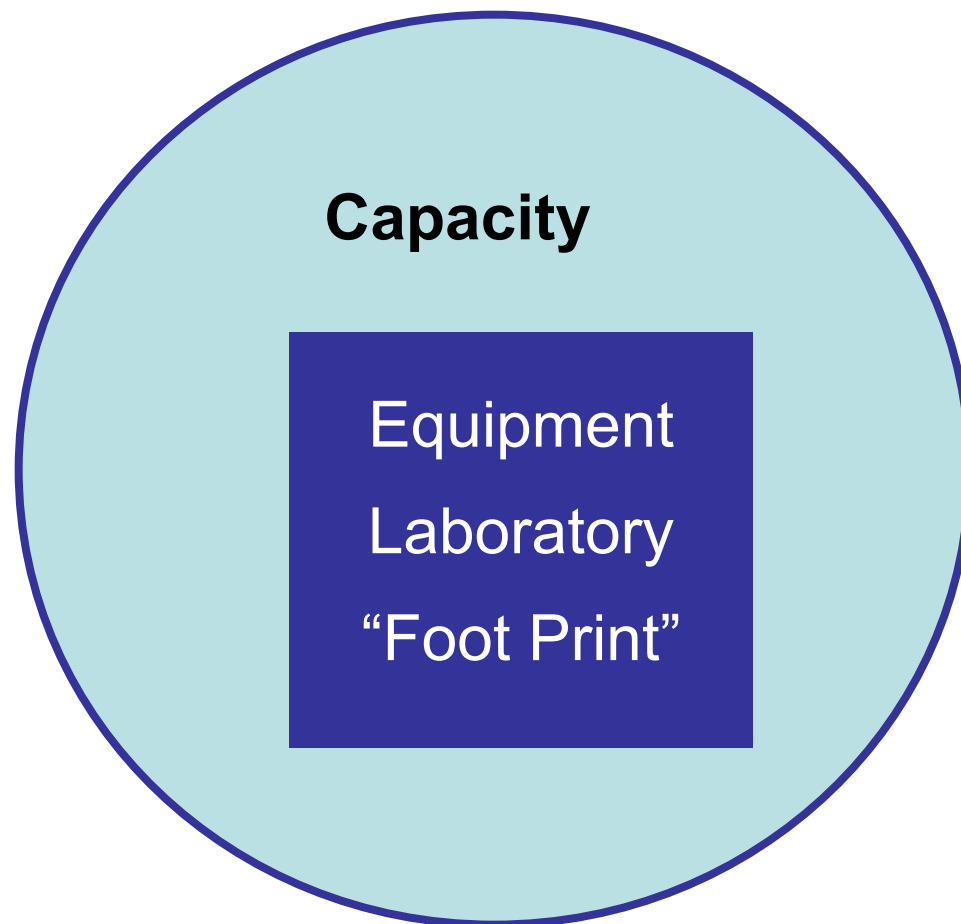
- ✓ Preparation
- ✓ Formulation
- ✓ Fill, Lyophilization, & Cap
- ✓ Packaging

Laboratory

- ✓ Environmental monitor
- ✓ Product specific test
- ✓ Compendial testing

“Foot Print”

- ✓ Multiple lines
- ✓ Aseptic areas
- ✓ Waste treatment
- ✓ Supporting equipment and processes



Vial to Pre-filled Syringe:

Why? Value Proposition

- Market – differentiation, premium pricing
- Customer – safety, accurate dosing, self-administration
- Product – less API waste → more units filled

What? Regulatory Strategy

- Evaluate and compare syringe system to current presentation
- Need supporting clinical data?
- Perform stability study

Vial to Pre-filled Syringe:

How? Vial to Syringe

- Container/Closure - extractables/leachables
- Formulation – liquid to liquid? Lyo to liquid?
- Storage Conditions – stability study, degradation profile
- Filing – clinical study? Stability supporting data

Who? CMO requirements

- Experience
- Capability
- Qualification
- Capacity

References

¹*Moving to a Pre-Filled Syringe: Stability Considerations – A Regulatory Perspective*. Raenel Gibson, RAC Regulatory Affairs Manager, Baxter Pharmaceutical Solutions LLC. Presented at the PDA “The Universe of Pre-filled Syringes and Injection Devices”, San Diego, CA, October 6-7, 2008.

²*Financial Model For Converting From a Vial To a Pre-filled Syringe*. Michael Borlet, Director of Marketing, Baxter Pharmaceutical Solutions LLC. Presented at the PDA “The Universe of Pre-filled Syringes and Injection Devices”, San Diego, CA, October 6-7, 2008.

Copaxone is a registered trademark of Teva Pharmaceutical Industries Ltd.

Baxter is a trademark of Baxter International Inc.

Enbrel is a trademark of Immunex Corporation

PFS is a trademark of Pharmacia & Upjohn Company

SureClick is a trademark of Amgen Inc.

Shoot for Share: From Vial to Pre-Filled Syringe

- Thank you for participating in this complimentary webinar.
- If you have further questions or would like to contact me:

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