

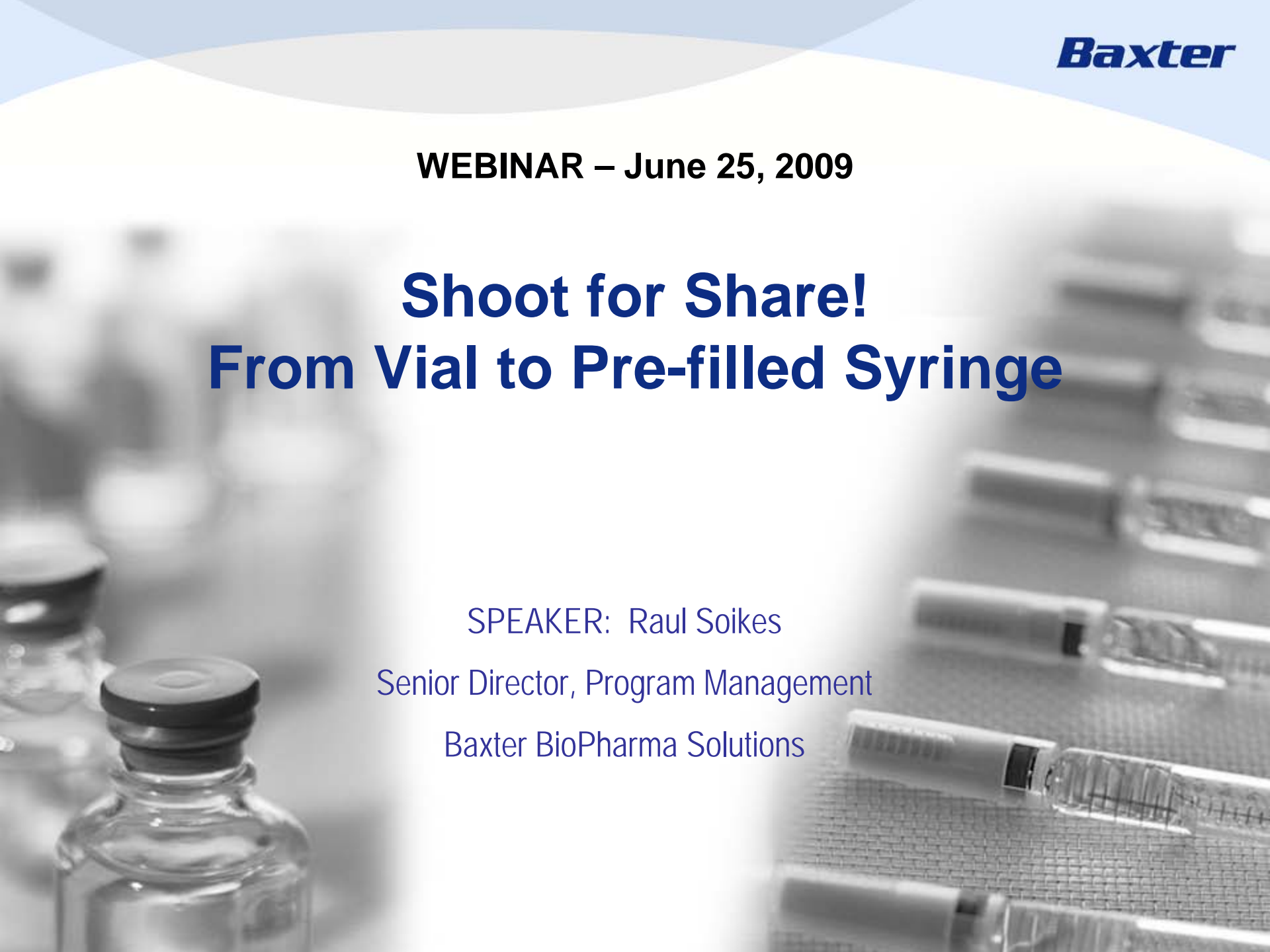
**WEBINAR – June 25, 2009**

# **Shoot for Share! From Vial to Pre-filled Syringe**

**SPEAKER: Raul Soikes**

**Senior Director, Program Management**

**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

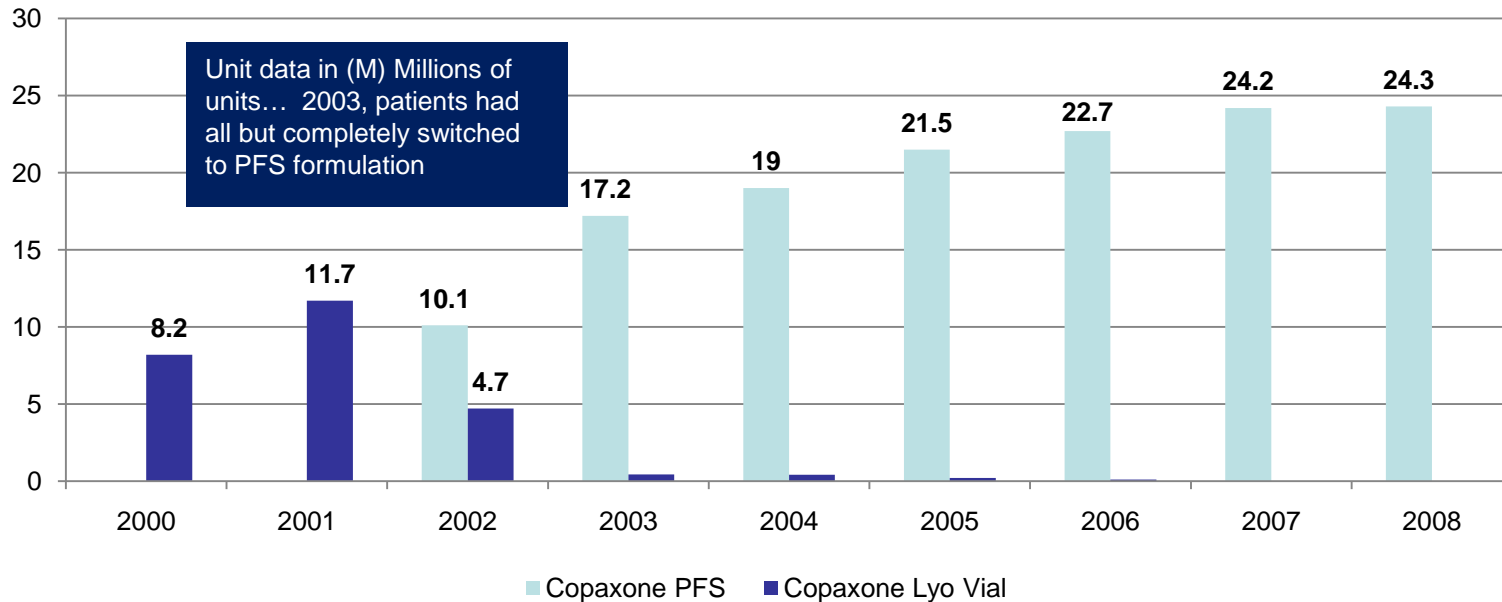
Due to the inherent challenges of biologics, enhancements are difficult yet the market rewards improvements

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.



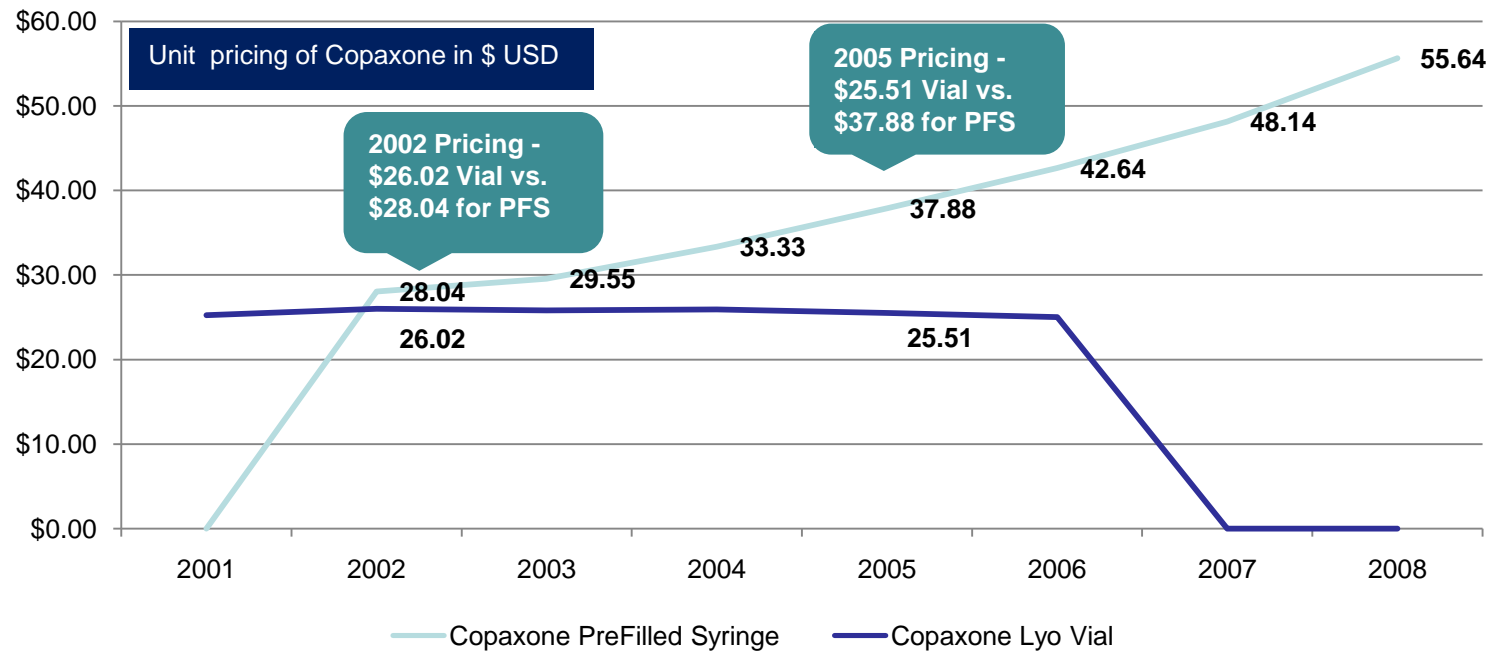
Copaxone PFS achieved rapid uptake in the US, with 64% of patients switching within the first three months from the dry vial formulation to the new formulation, and the remainder had switched within six months of launch.

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

# Why? - Mid-Term Strategy



The Copaxone<sup>®</sup> 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.

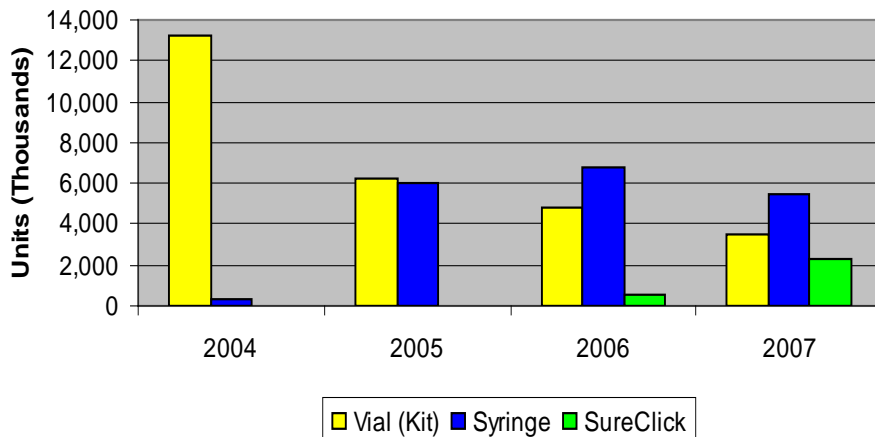
Premium pricing - from 5% in 2002 to 49% by 2005.

Preparation time reduced from 4 minutes to 38 seconds.

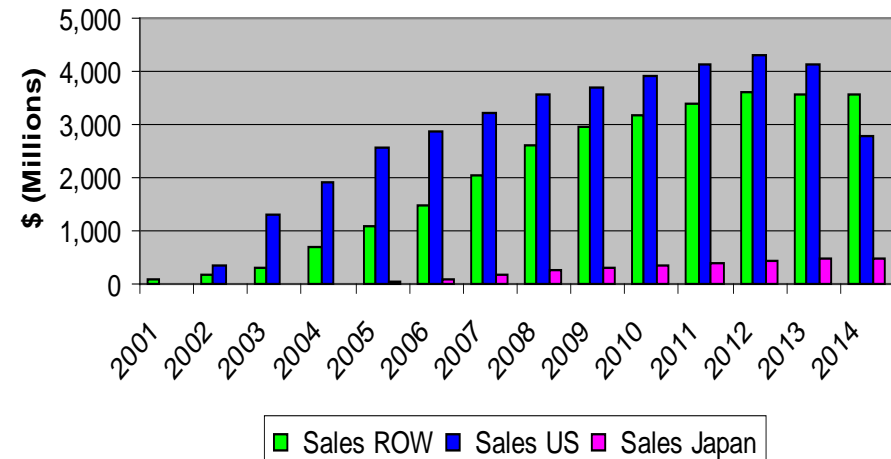
# Why? - Mid-Term Strategy

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



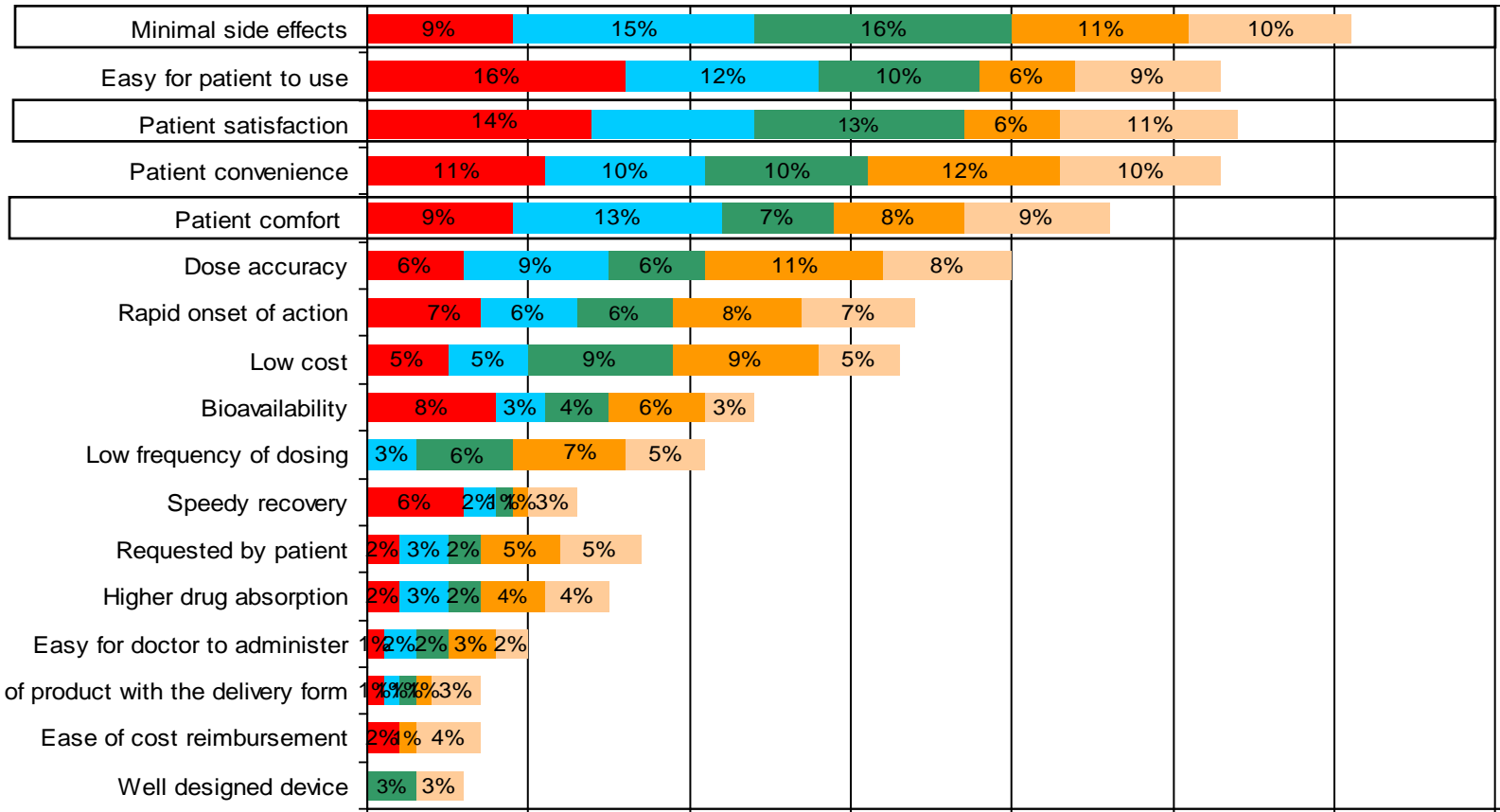
Overall Enbrel unit sales have remained stable, however revenue has increased due to the price premium the PFS and SureClick™ format.

Revenue increased due to price premium; unit sales stable

# Why? - Selecting a Drug Delivery Type



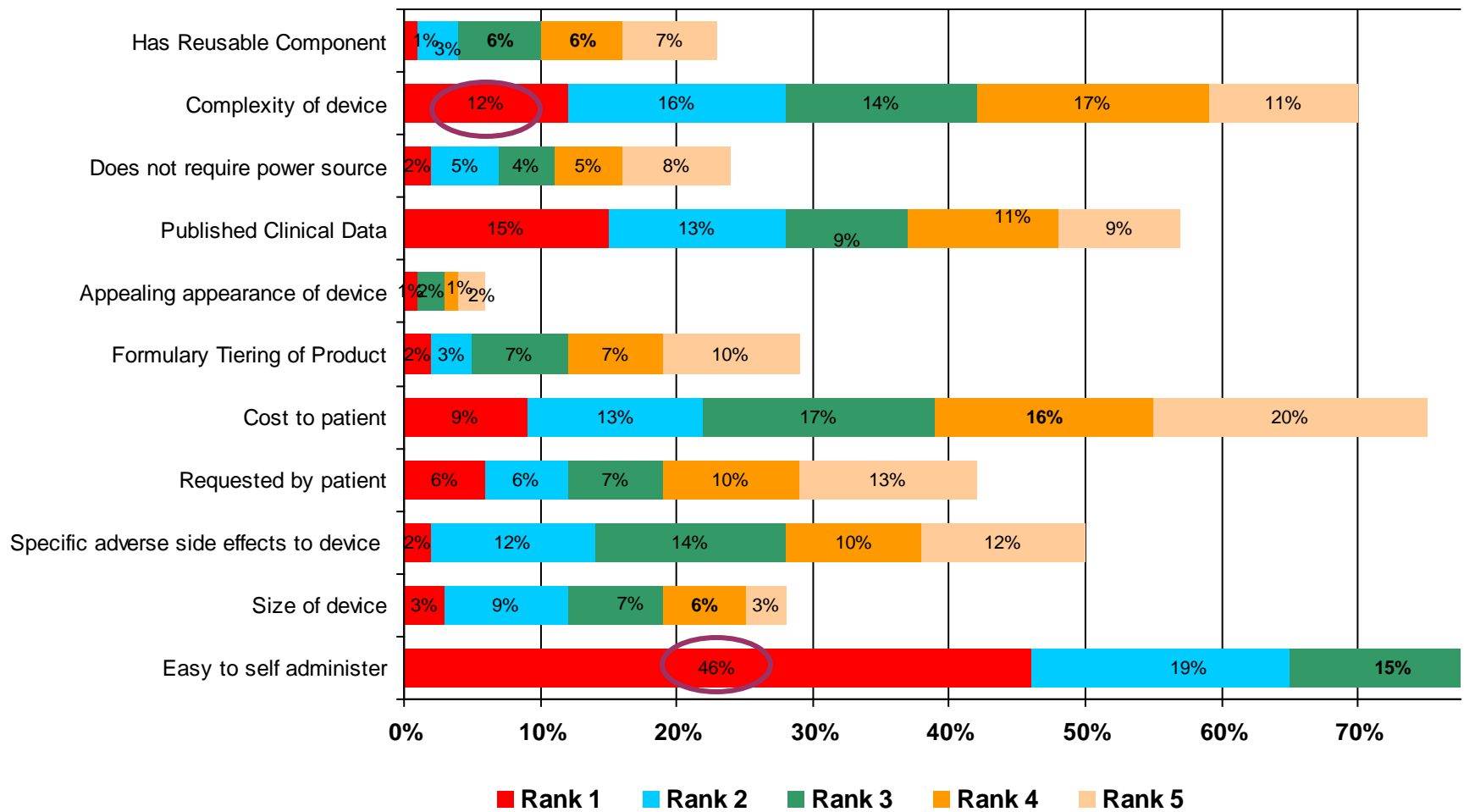
**Doctors' top factors : minimal side effects, patients ease of use, satisfaction, convenience, comfort. Three of five factors (underlined) impacted by product presentation.**



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

# Why? Selecting Drug Delivery Type - Physician *Baxter*

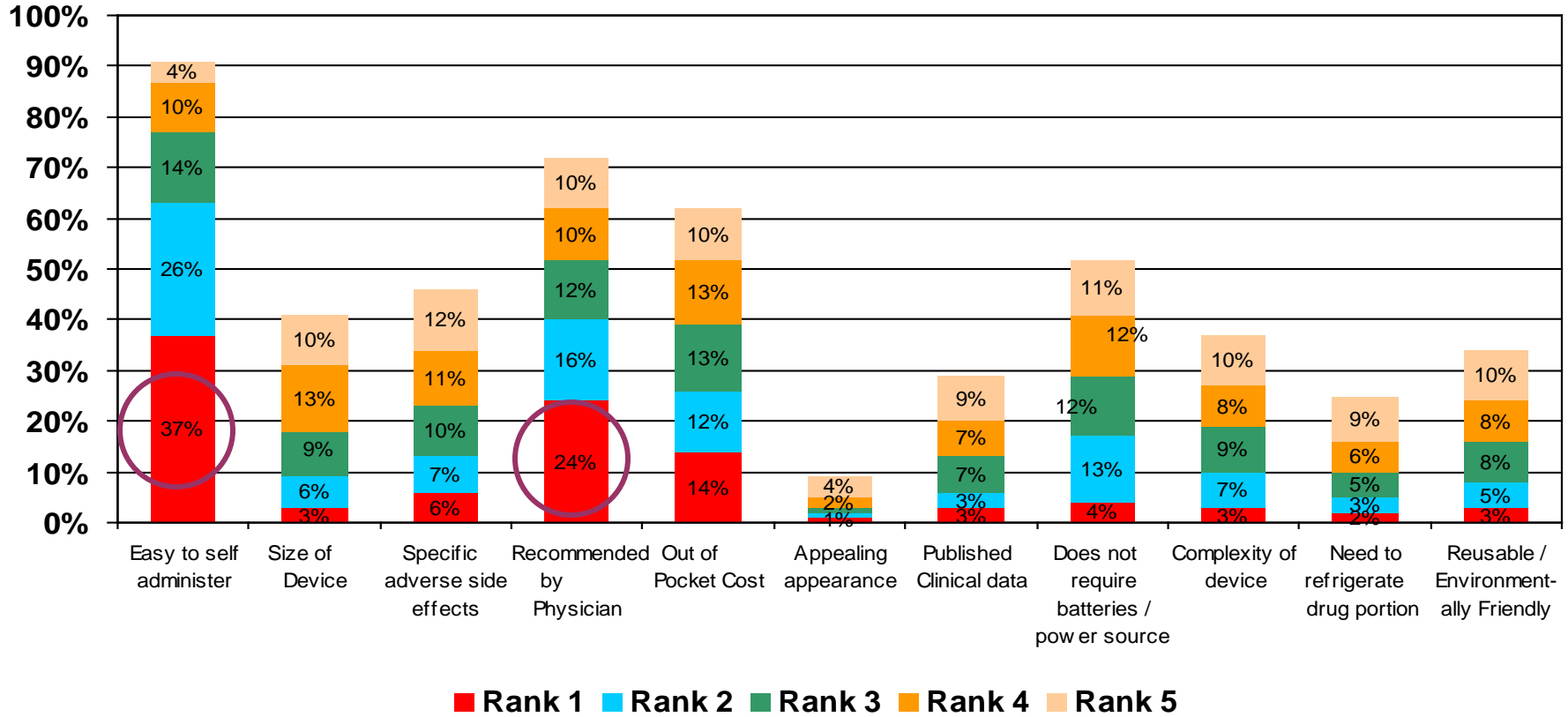
**Ease of self administering is the top reason for selecting a device type.**



**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

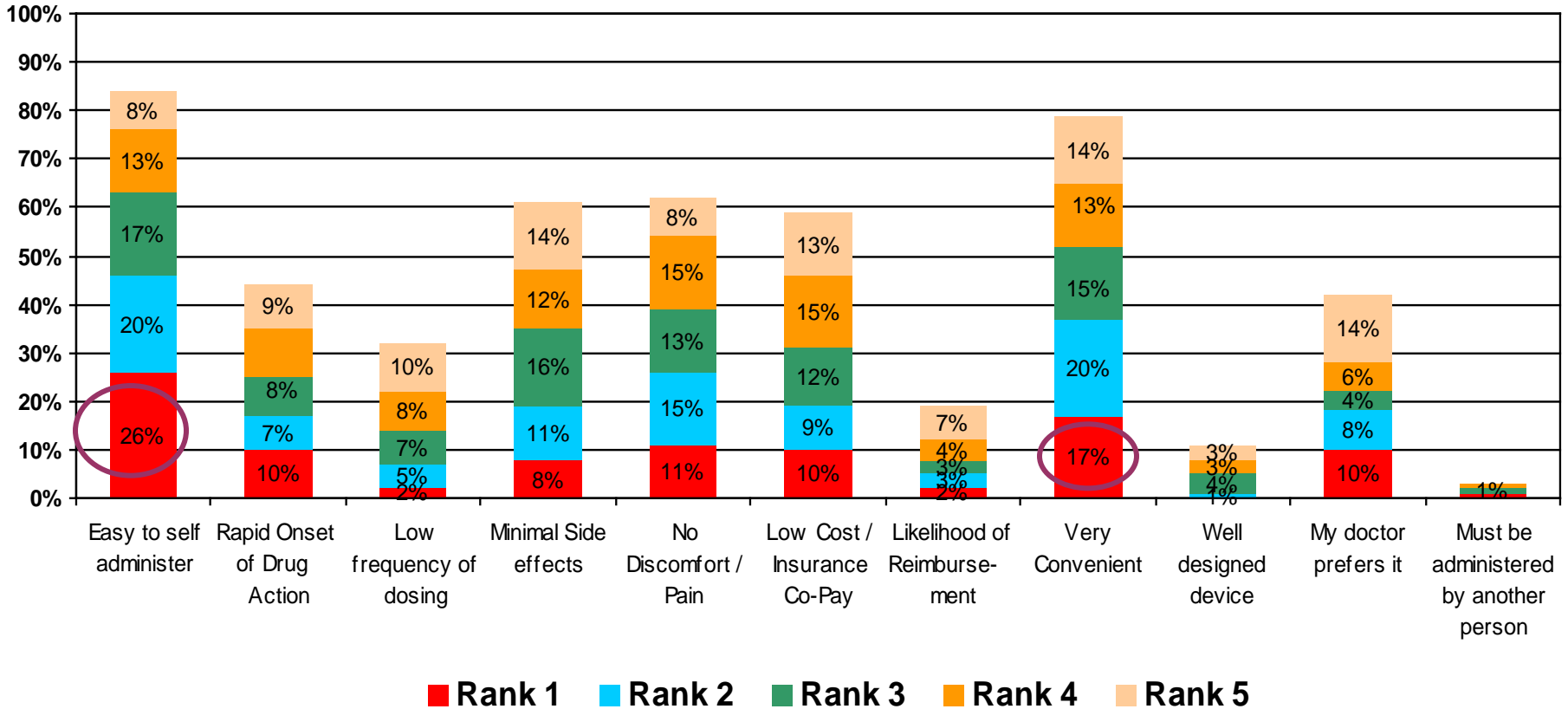
**Top Factors are ease of self administration (37%) followed by Physician's recommendation (24%)**



**Question:**  
**For Device Driven Drug Delivery what are the top 5 factors that you consider? (1=most important, 2=2<sup>nd</sup> most important, 3=3<sup>rd</sup> 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=2<sup>nd</sup> most important, 3=3<sup>rd</sup> 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

- ✓ Protects the drug product?
- ✓ Introduce a new material?
- ✓ Need drug product formulation changes?

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

# What?

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

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

# What?

<b>Define Regulatory Strategy</b>		
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"> <li>✓ Protects the drug product?</li> <li>✓ Introduce a new material?</li> <li>✓ Need drug product formulation changes?</li> </ul>	<ul style="list-style-type: none"> <li>✓ Safety or efficacy effect?</li> <li>✓ New indication?</li> <li>✓ New route of administration?</li> </ul>	<ul style="list-style-type: none"> <li>✓ Define stability requirements</li> <li>✓ Execute stability protocol</li> <li>✓ Analyze stability data</li> </ul>

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

**HOW?**

VIAL TO SYRINGE

**How?**

**REGULATORY STRATEGY**

**Formulation  
Study**

**Stability  
Study**

**Clinical  
Study**

**Filing**

**How?**

**REGULATORY STRATEGY**

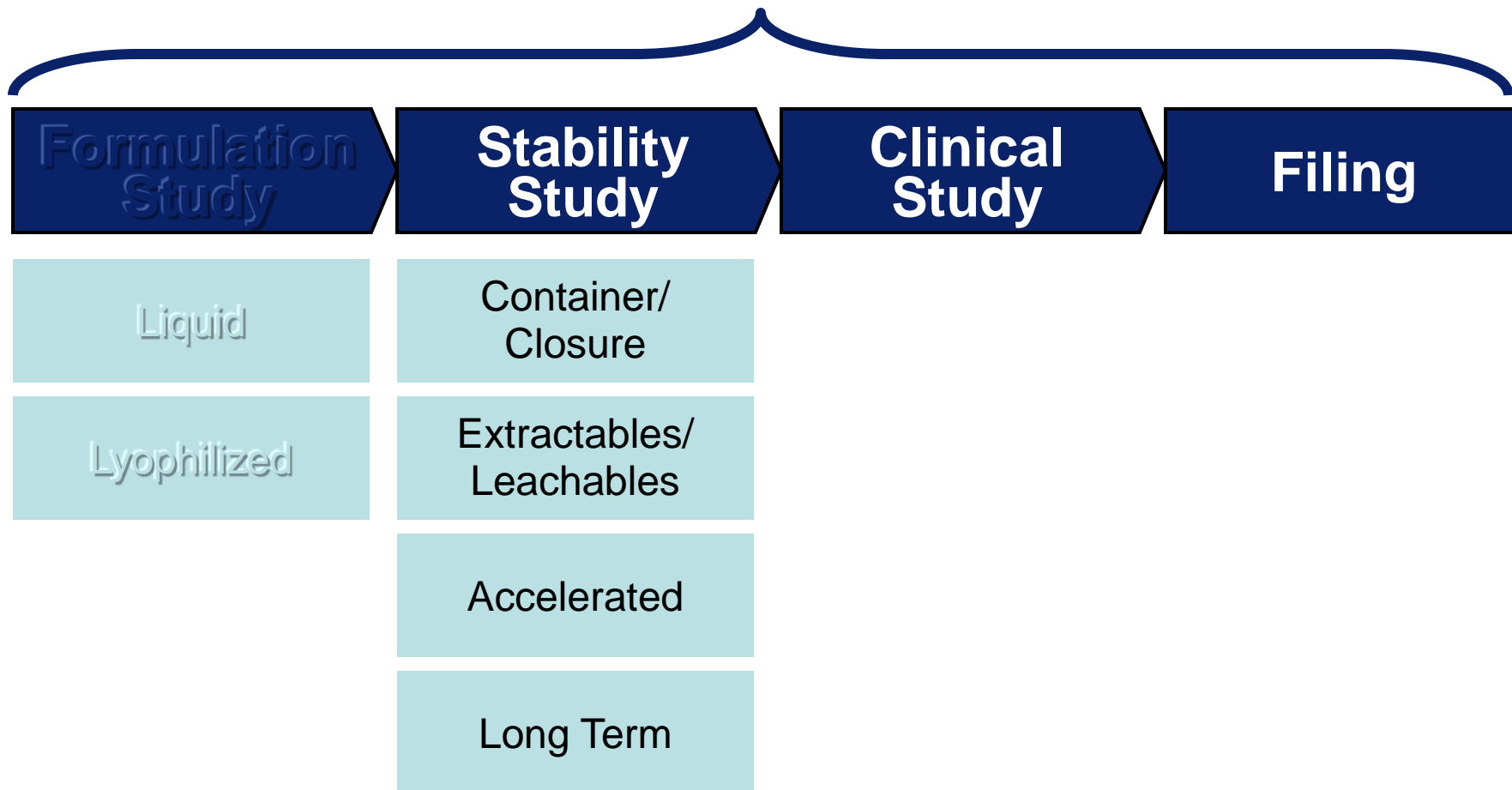


Liquid

Lyophilized

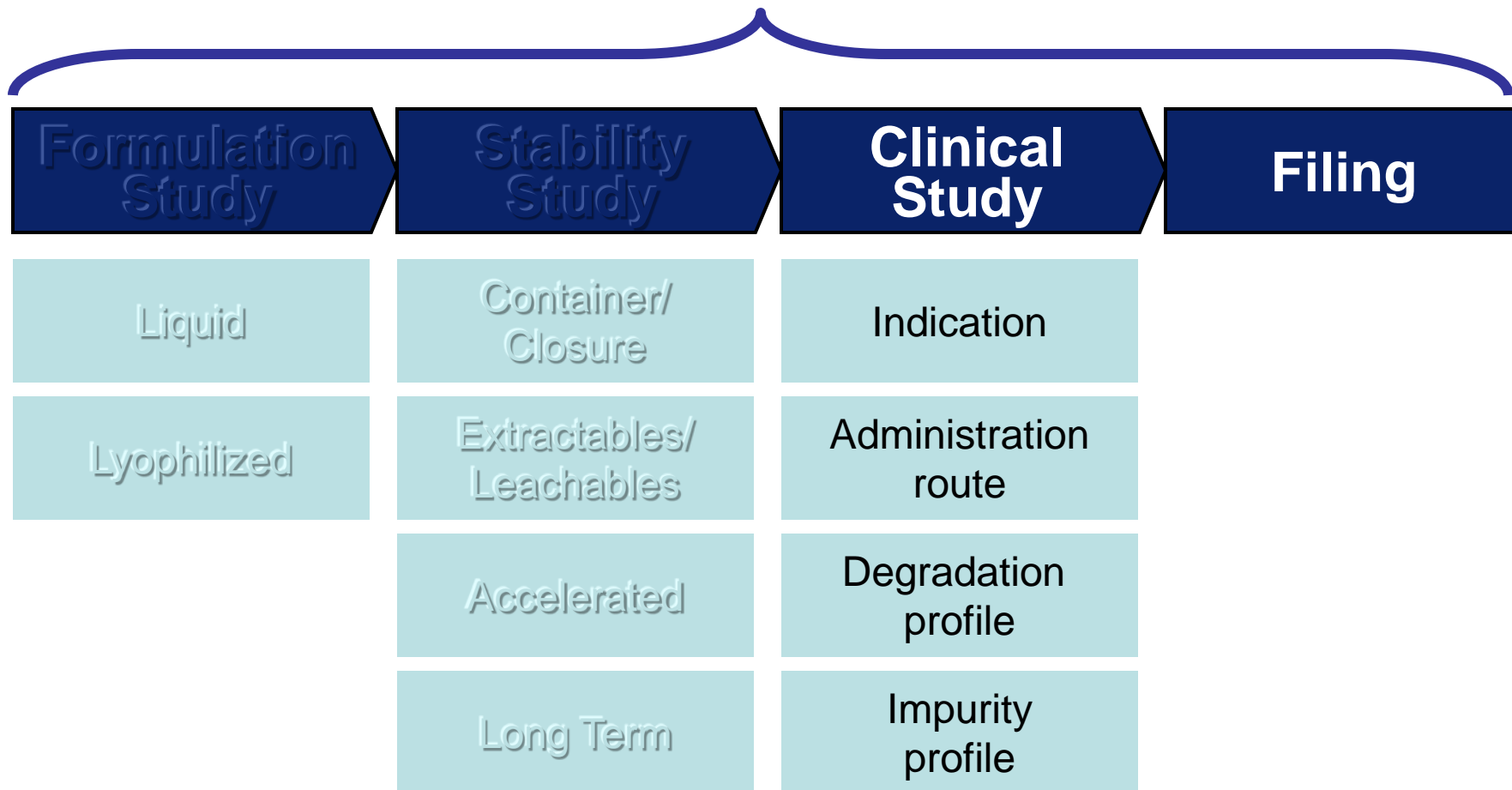
**How?**

**REGULATORY STRATEGY**



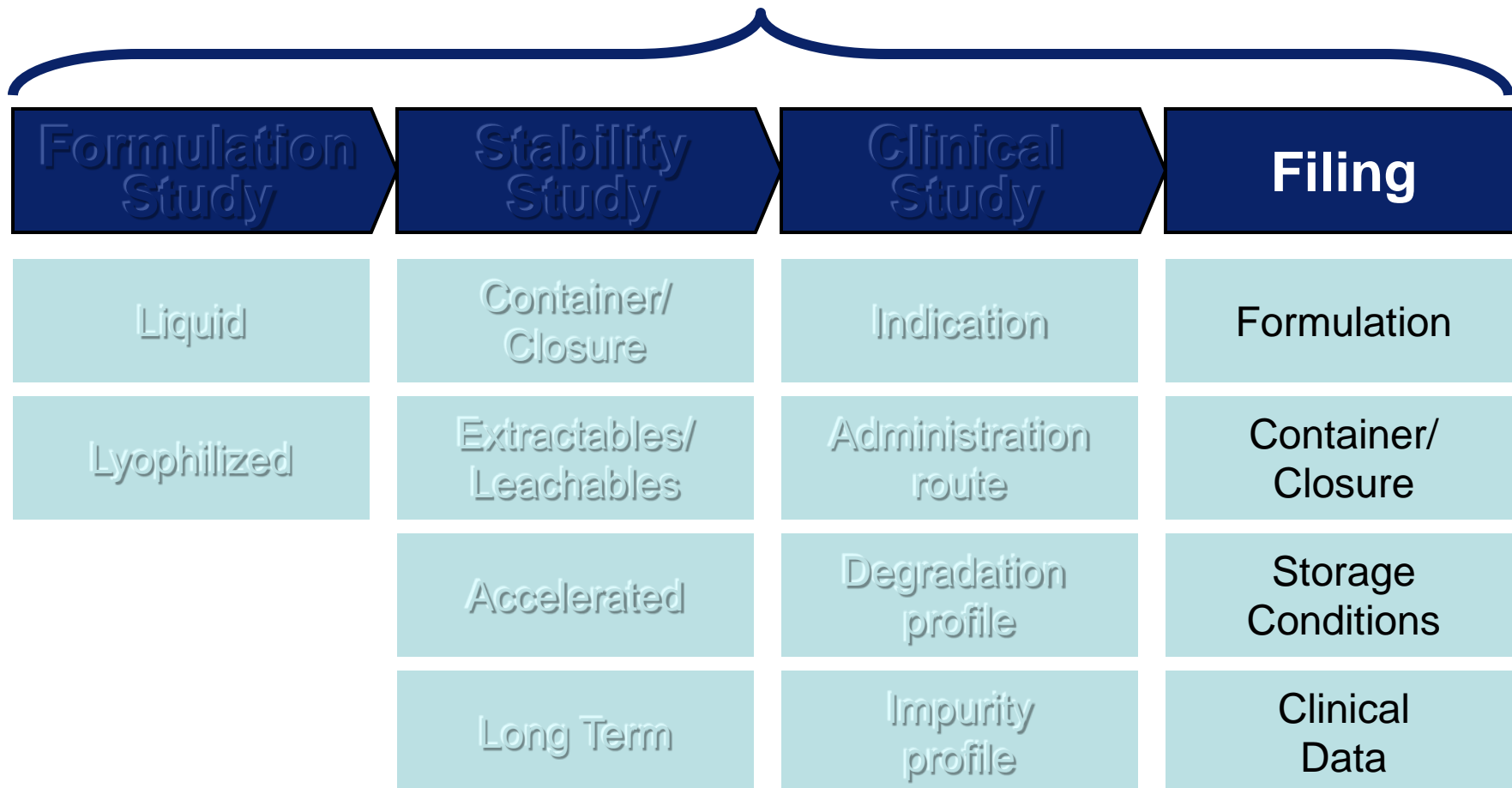
# How?

## REGULATORY STRATEGY



**How?**

**REGULATORY STRATEGY**



## How?

### Pre-filled syringe filing details:

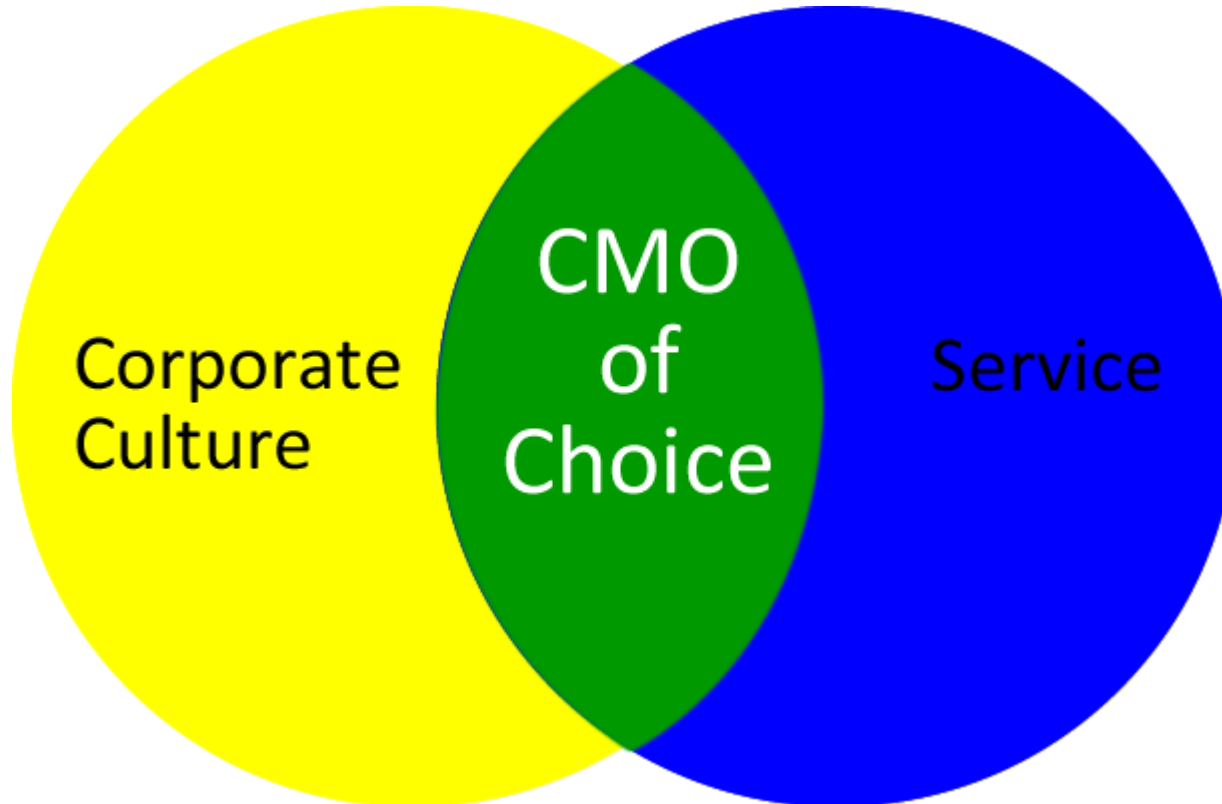
Attribute*	Move From Liquid Vial	Move From Lyo Vial
Container/Closure	Similar? Leverage previous extractable/leachable studies. Functionality: siliconization may be needed.	
Formulation	No change.	Change from freeze-dried powder to liquid.
Storage Conditions	No change.  <u>Stability Study</u> : 3 months 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

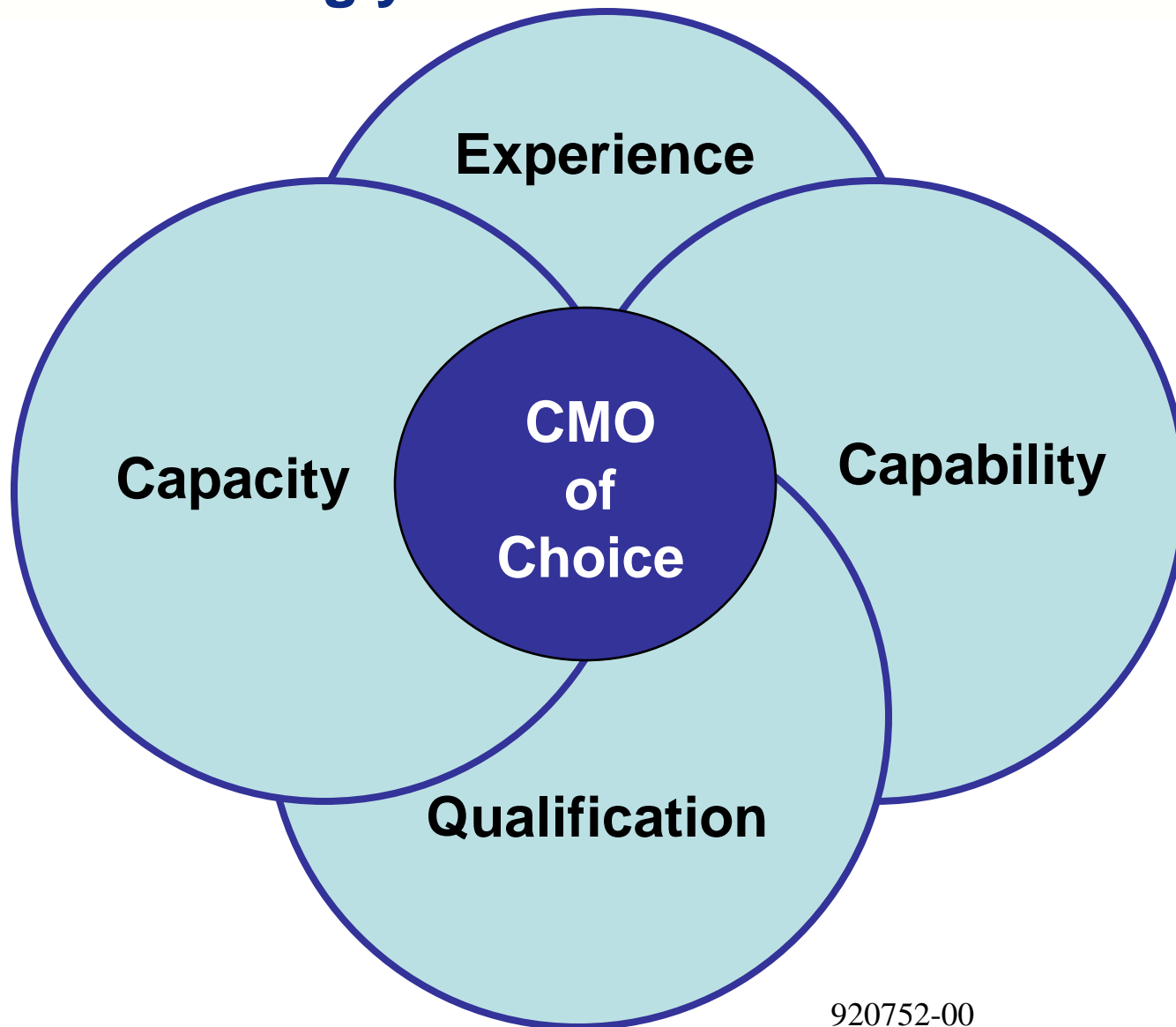
**WHO?**

**CMO REQUIREMENTS**

# Who?



## Who? Choosing your CMO . . .



# Experience

## Regulatory

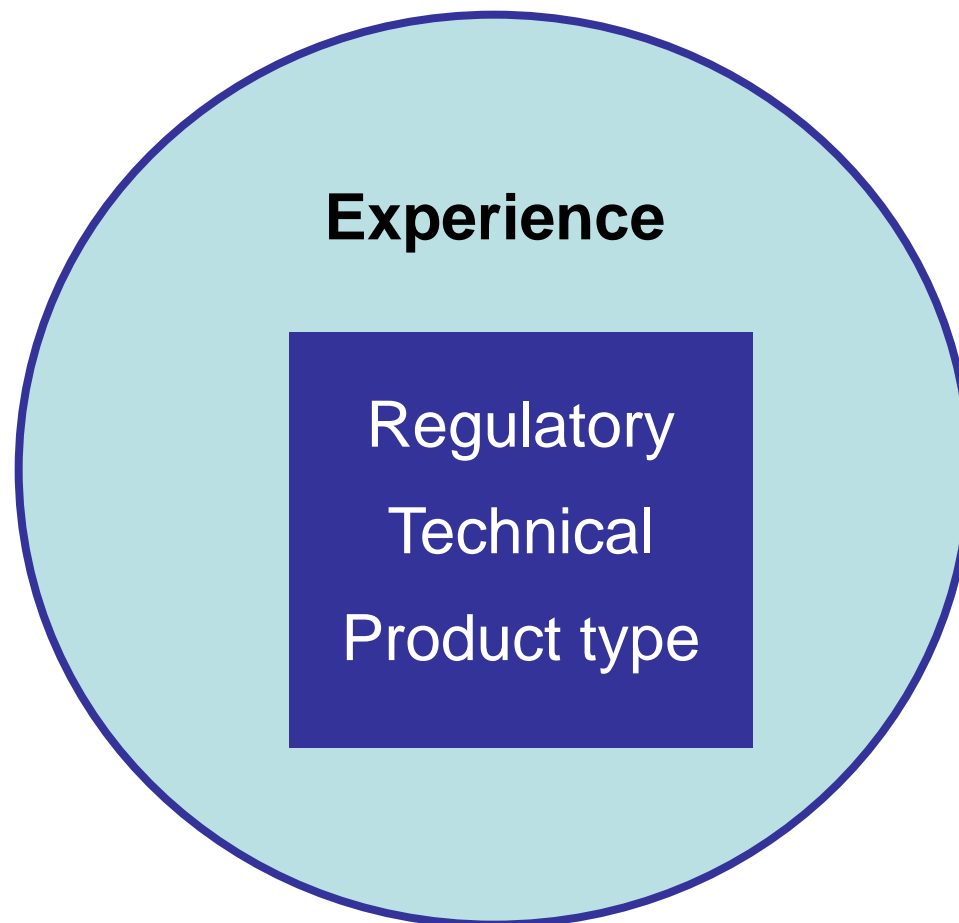
- ✓ Global and local compliance
- ✓ Audit history
- ✓ Regulatory review and approval process

## Technical

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

## Product Type

- ✓ Small Molecules
- ✓ Biologicals



# Capability

## Resources

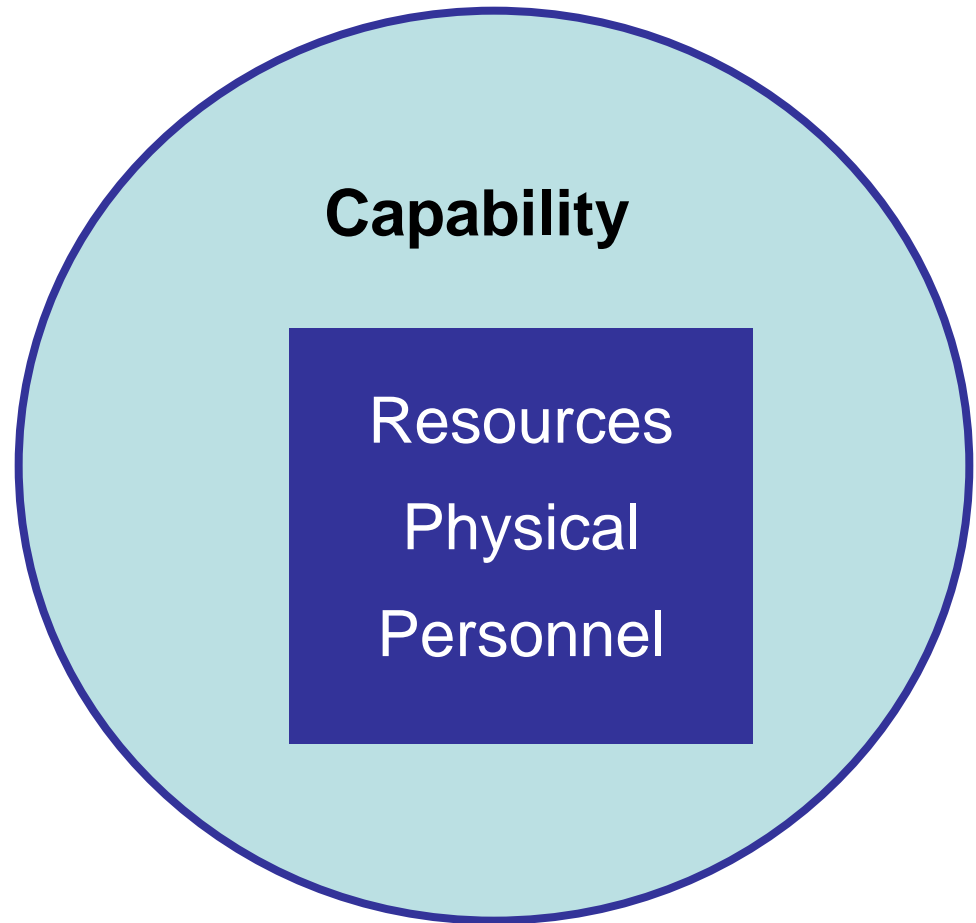
- ✓ Part of global company
- ✓ Redundancy
- ✓ Multidisciplinary

## 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

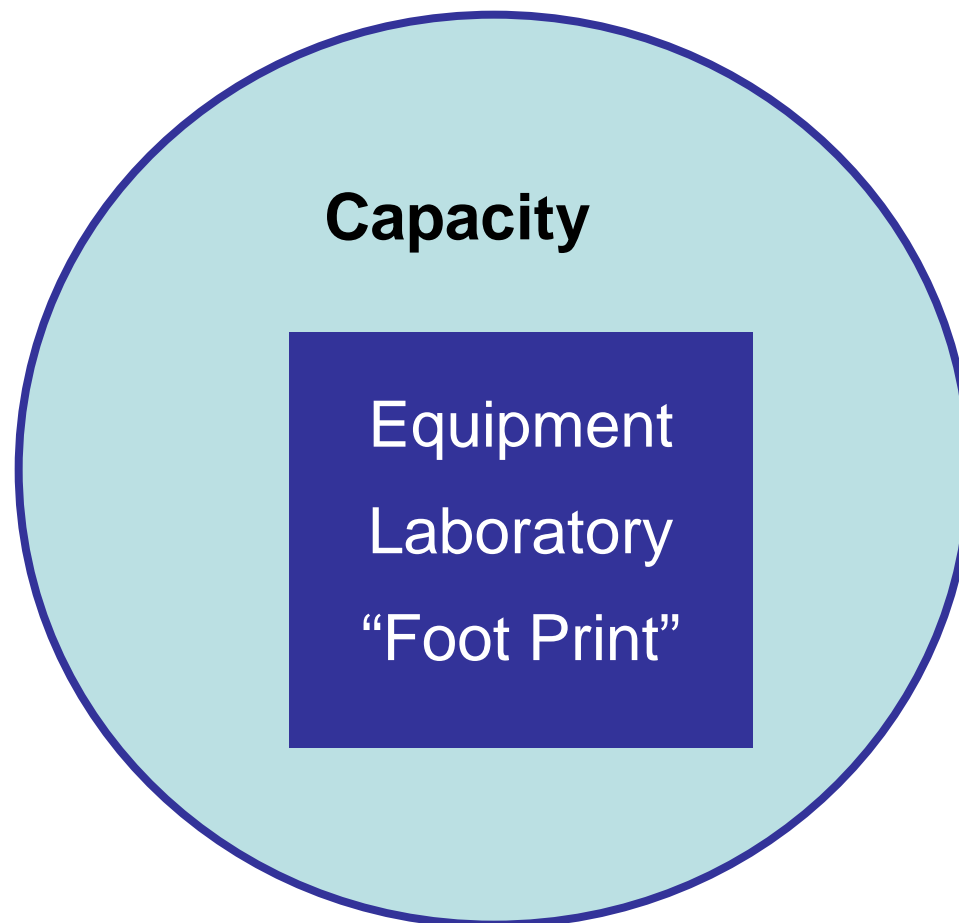
- ✓ Preparation
- ✓ Formulation
- ✓ Fill, Lyophilization, & Cap
- ✓ Packaging

## 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

<sup>1</sup>*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.

<sup>2</sup>*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.

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## 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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