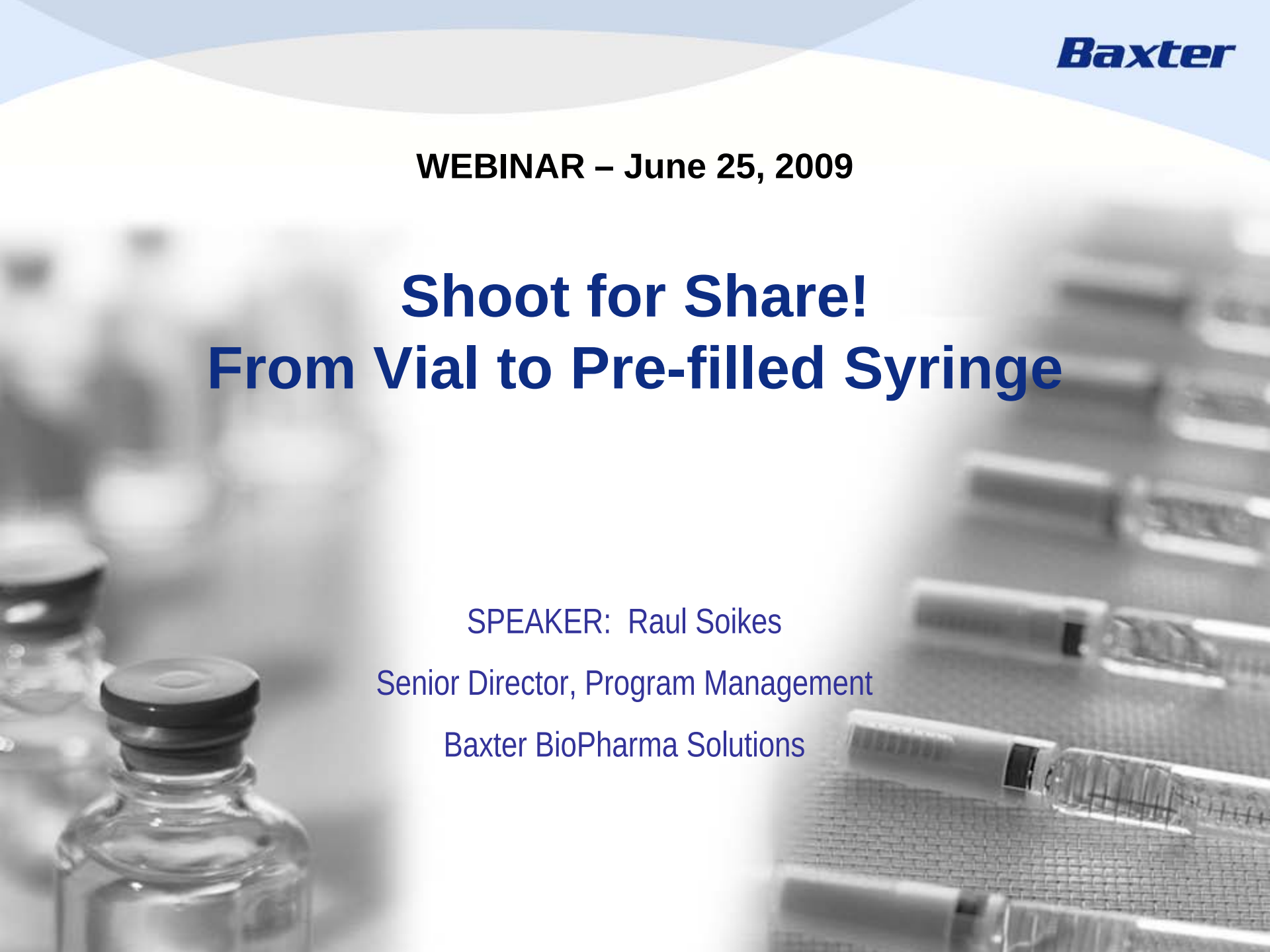
WEBINAR – June 25, 2009

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

Baxter

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

Enhanced Packaging and Reformulation Give New Life to Biologics, Tom Polen, BioPharm International, October 2006

Why? - Mid-Term Strategy

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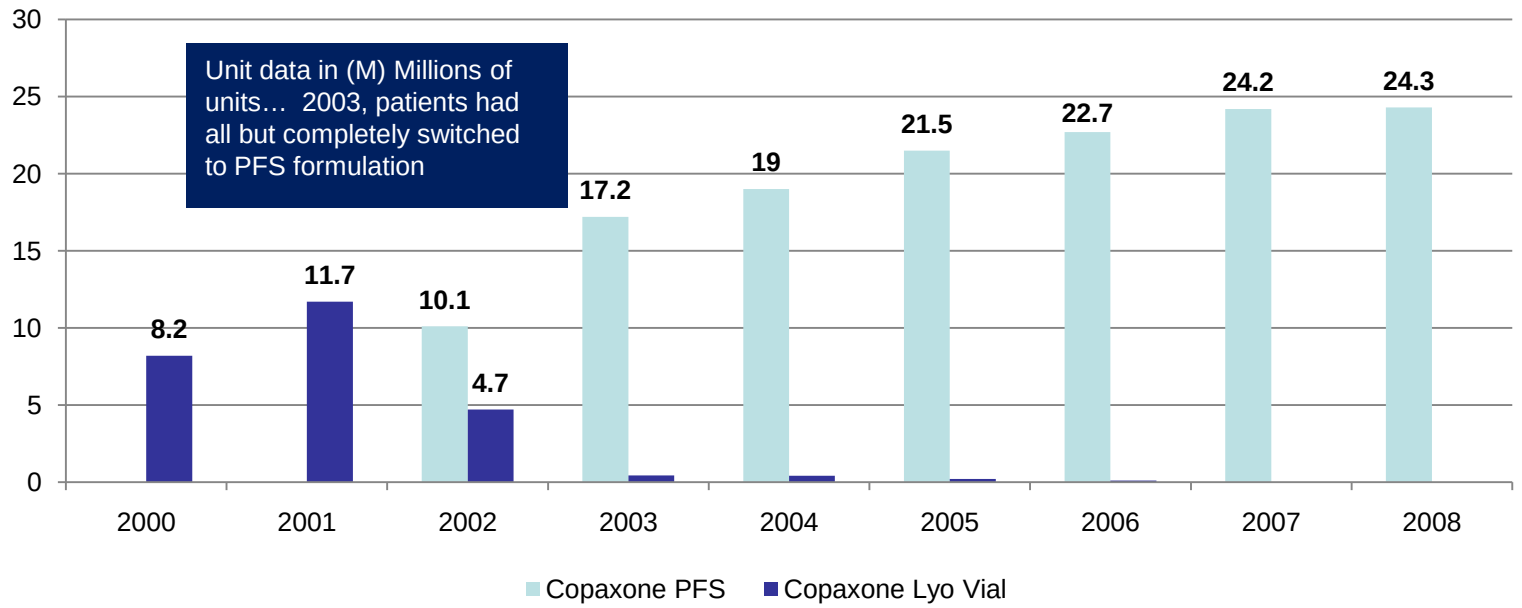
Teva Pharmaceutical Industries Ltd changes the presentation of Copaxone® from a dry vial preparation to a pre-filled syringe.



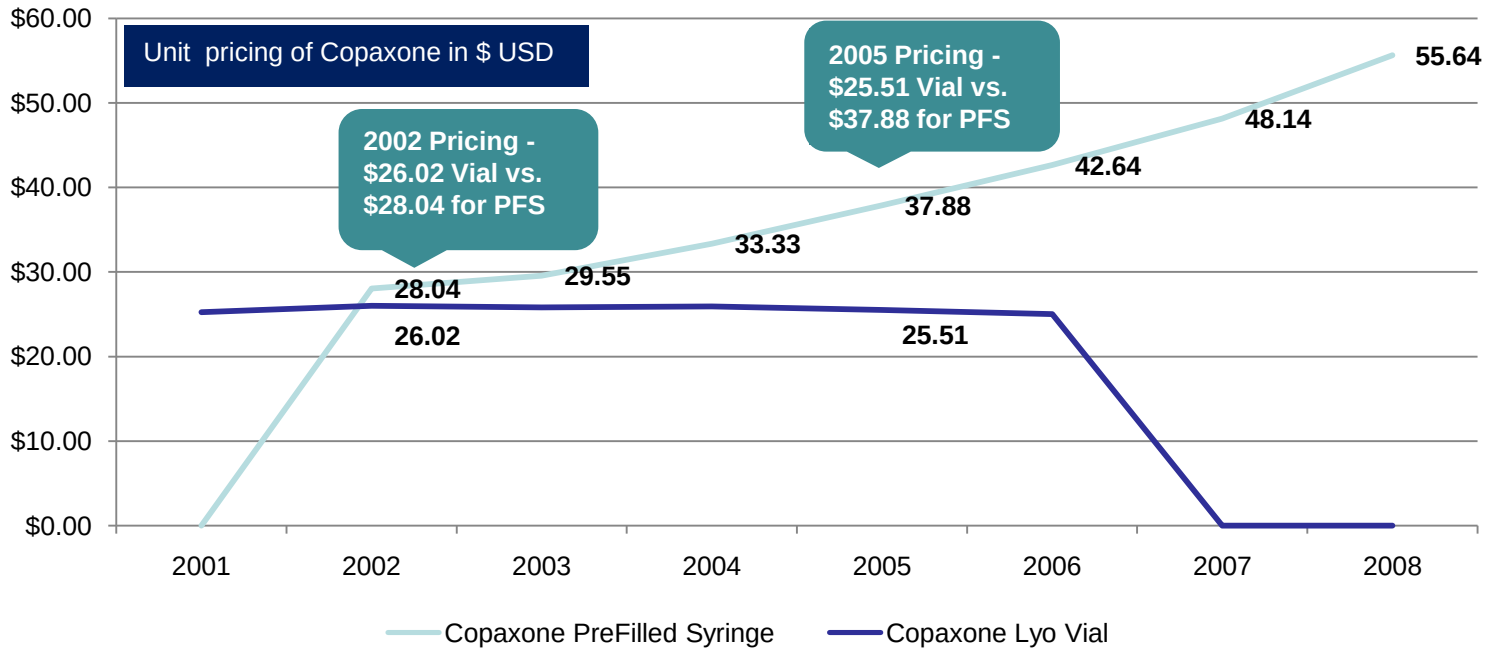
Copaxone PFS achieved rapid uptake in the US, with 64% of patients switching within the first three months from the dry vial formulation to the new formulation, and the remainder had switched within six months of launch.

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

Source: IMS Health

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.

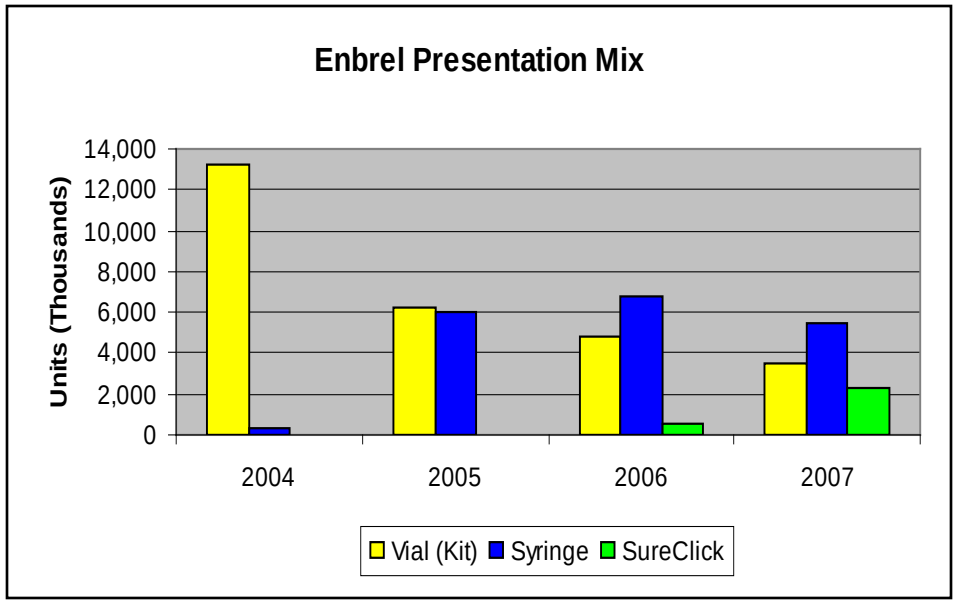
Premium pricing - from 5% in 2002 to 49% by 2005.

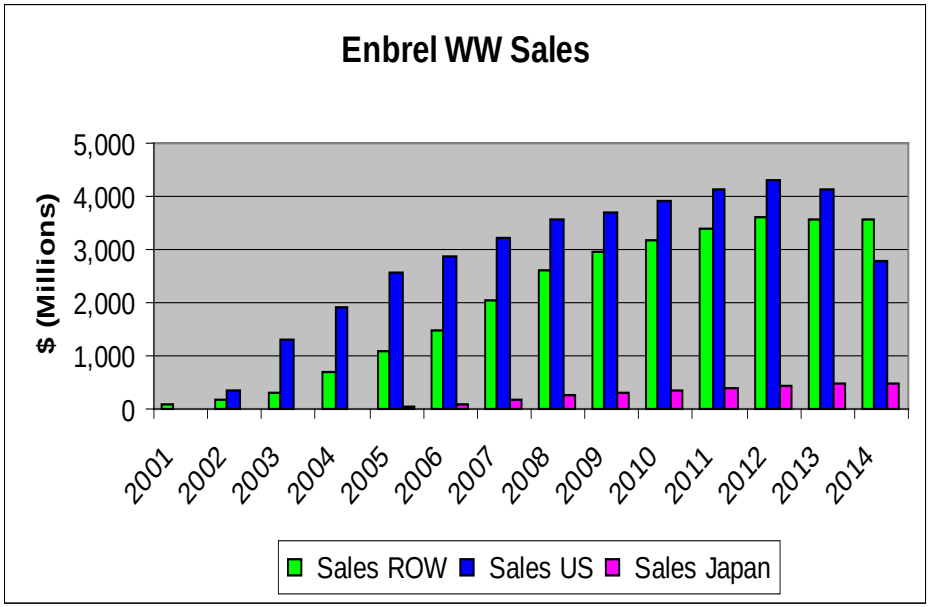
Preparation time reduced from 4 minutes to 38 seconds.

Source: IMS Health

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.





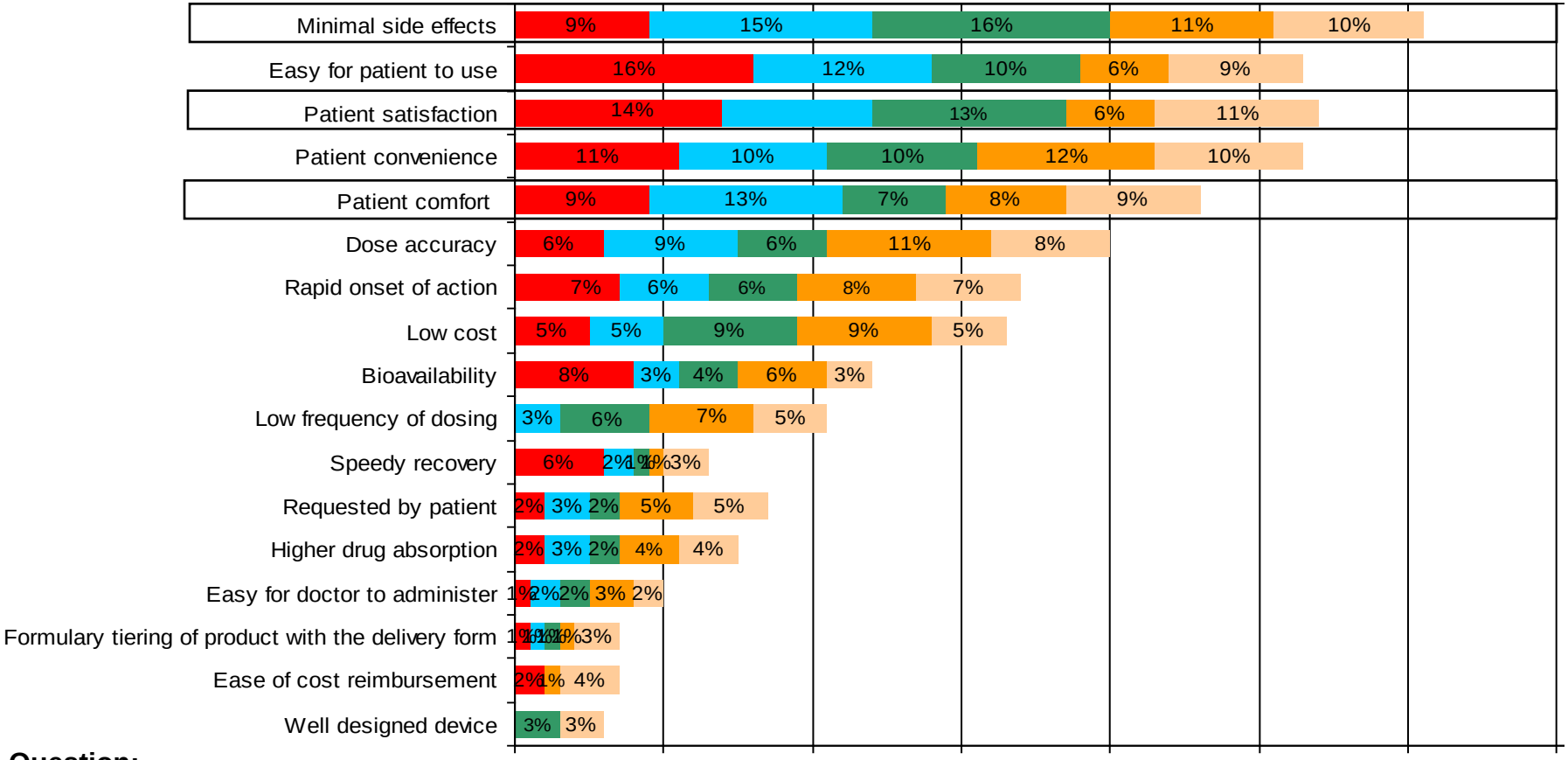
Overall Enbrel unit sales have remained stable, however revenue has increased due to the price premium the PFS and SureClick™ format.

Revenue increased due to price premium; unit sales stable

IMS Data

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.)

US Drug Delivery - Frost & Sullivan 2008

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Why? Selecting Drug Delivery Type - Physician

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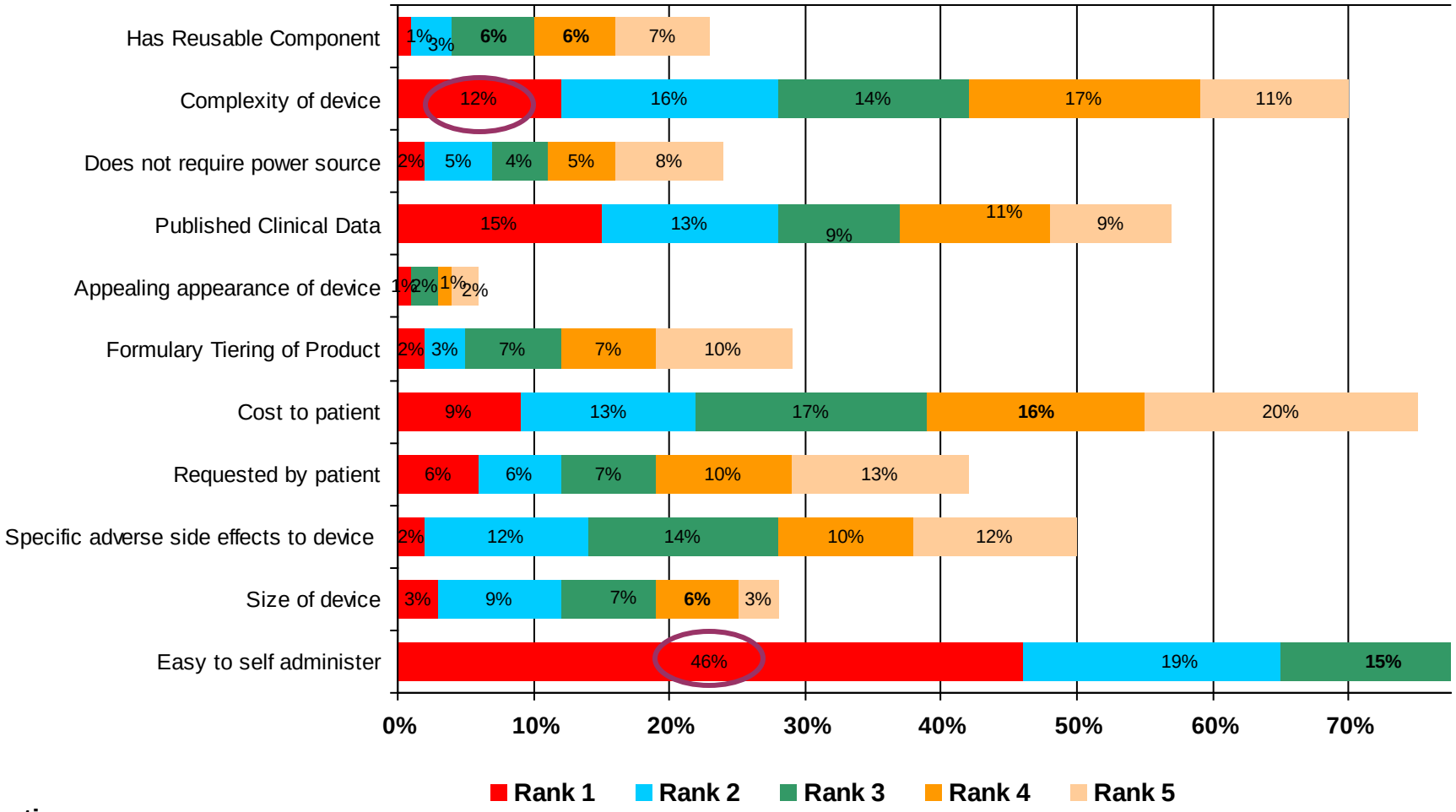
Ease of self administering is the top reason for selecting a device type.



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?

US Drug Delivery - Frost & Sullivan 2008

Why? Device Drug Delivery Method - Patient

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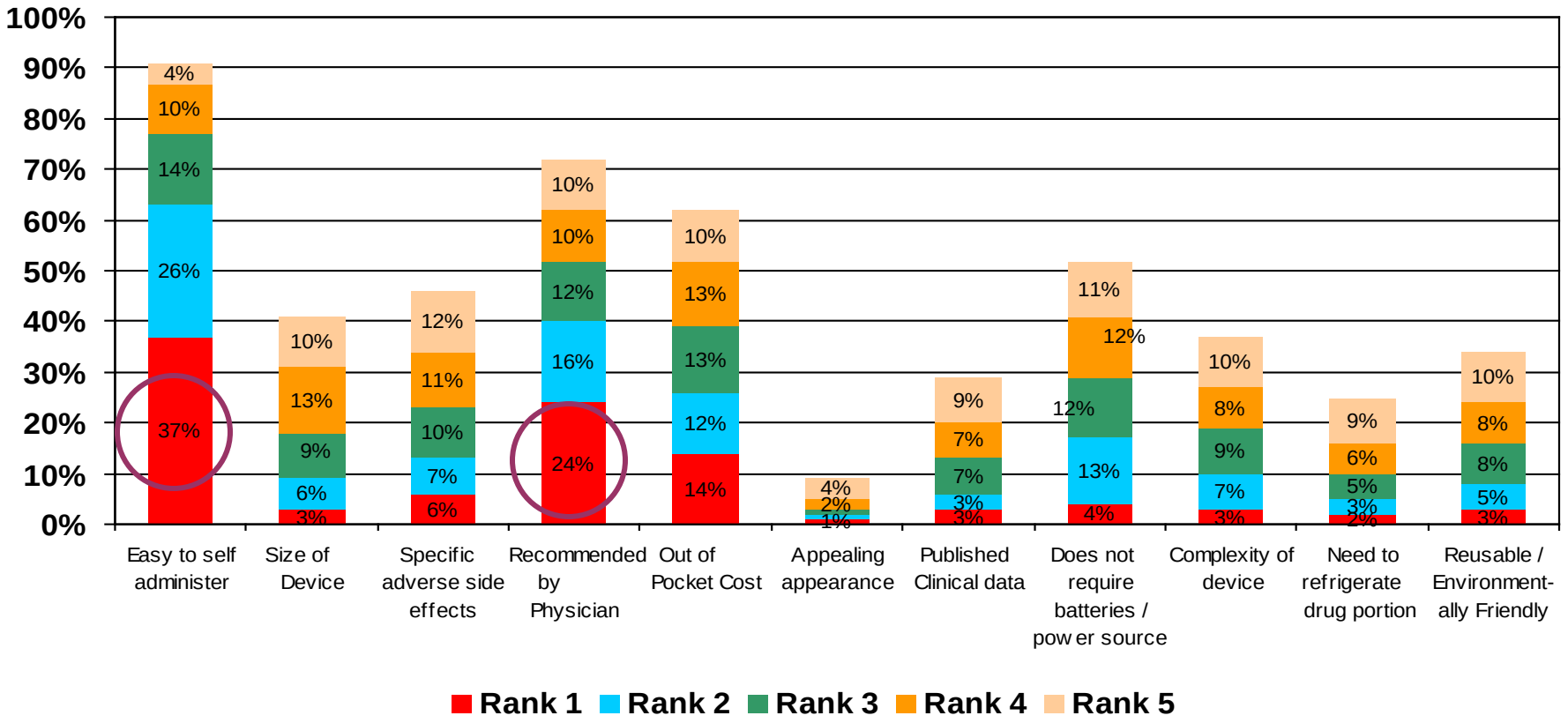
Top Factors are ease of self administration (37%) followed by Physician's recommendation (24%)

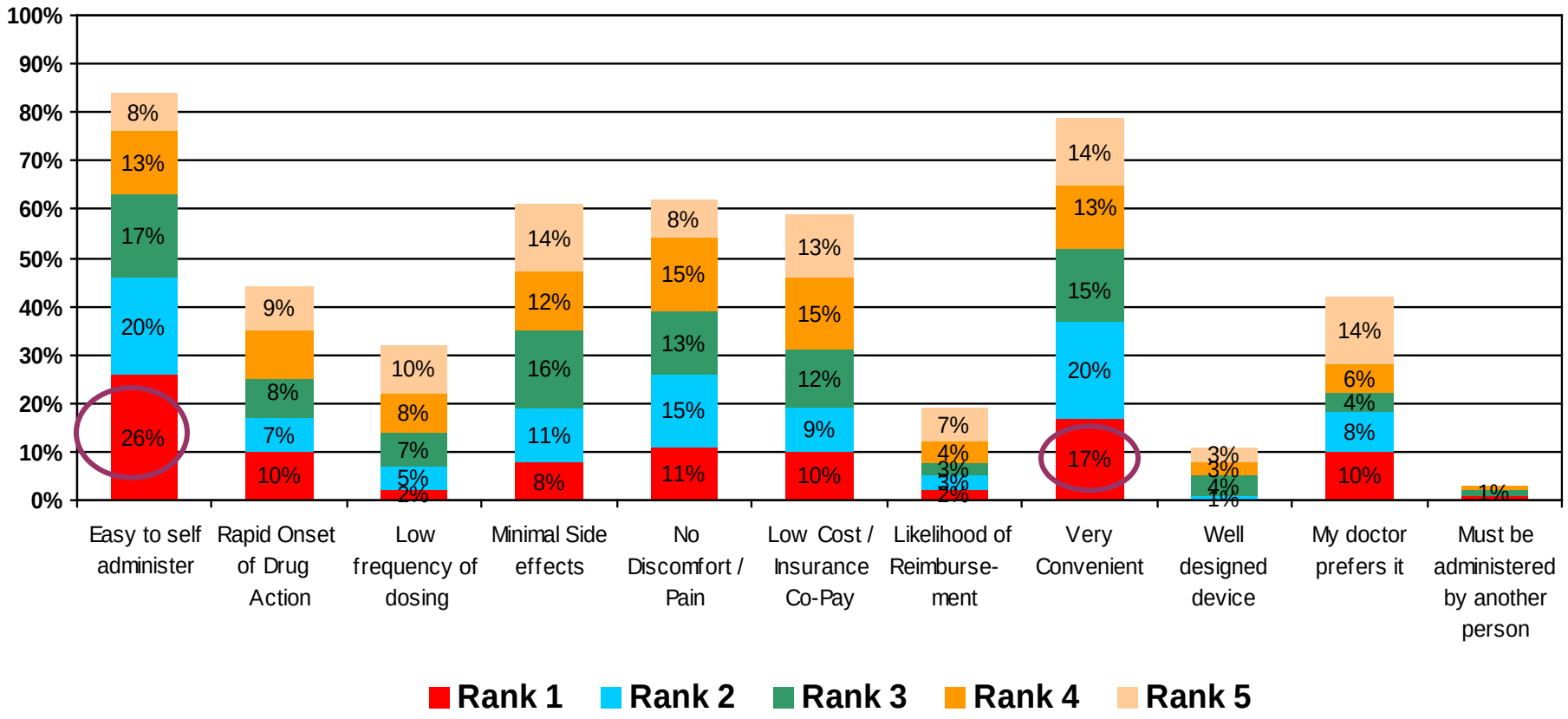


Question:
For Device Driven Drug Delivery what are the top 5 factors that you consider? (1=most important, 2=2nd most important, 3=3rd most important, etc.)

US Drug Delivery - Frost & Sullivan 2008

Why? Device Drug Delivery Method – Patient

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



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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.)

US Drug Delivery - Frost & Sullivan 2008

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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?

Define Regulatory Strategy		
Evaluate & compare the proposed syringe system to approved materials	Need supporting clinical data?	
✓Protects the drug product? ✓Introduce a new material? ✓Need drug product formulation changes?	✓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
✓Protects the drug product? ✓Introduce a new material? ✓Need drug product formulation changes?	✓Safety or efficacy effect? ✓New indication? ✓New route of administration?	✓Define stability requirements ✓Execute stability protocol ✓Analyze stability data

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

HOW?

VIAL TO SYRINGE

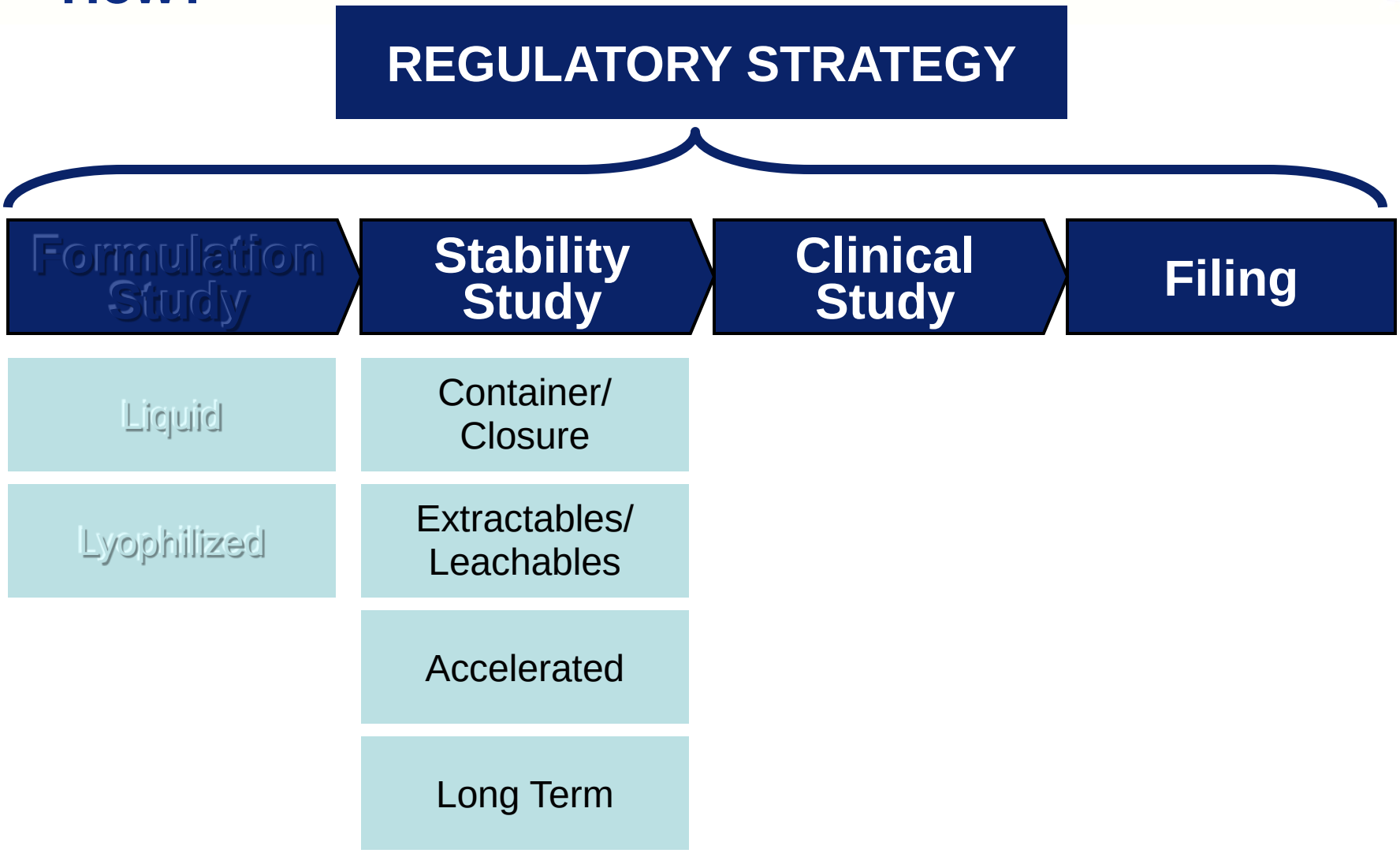
How?


REGULATORY STRATEGY
Formulation Study
Stability Study
Clinical Study
Filing

How?


REGULATORY STRATEGY
Formulation Study
Stability Study
Clinical Study
Filing
Liquid
Lyophilized

How?


REGULATORY STRATEGY
Formulation Study
Stability Study
Clinical Study
Filing
Liquid
Lyophilized
Container/ Closure
Extractables/ Leachables
Accelerated
Long Term

How?

REGULATORY STRATEGY

Formulation Study	Stability Study	Clinical Study	Filing
Liquid	Container/ Closure	Indication	
Lyophilized	Extractables/ Leachables	Administration route	
	Accelerated	Degradation profile	
	Long Term	Impurity profile	

How?

REGULATORY STRATEGY

Formulation Study	Stability Study	Clinical Study	Filing
Liquid	Container/ Closure	Indication	Formulation
Lyophilized	Extractables/ Leachables	Administration route	Container/ Closure
	Accelerated	Degradation profile	Storage Conditions
	Long Term	Impurity profile	Clinical Data

How?

Pre-filled syringe filing details:

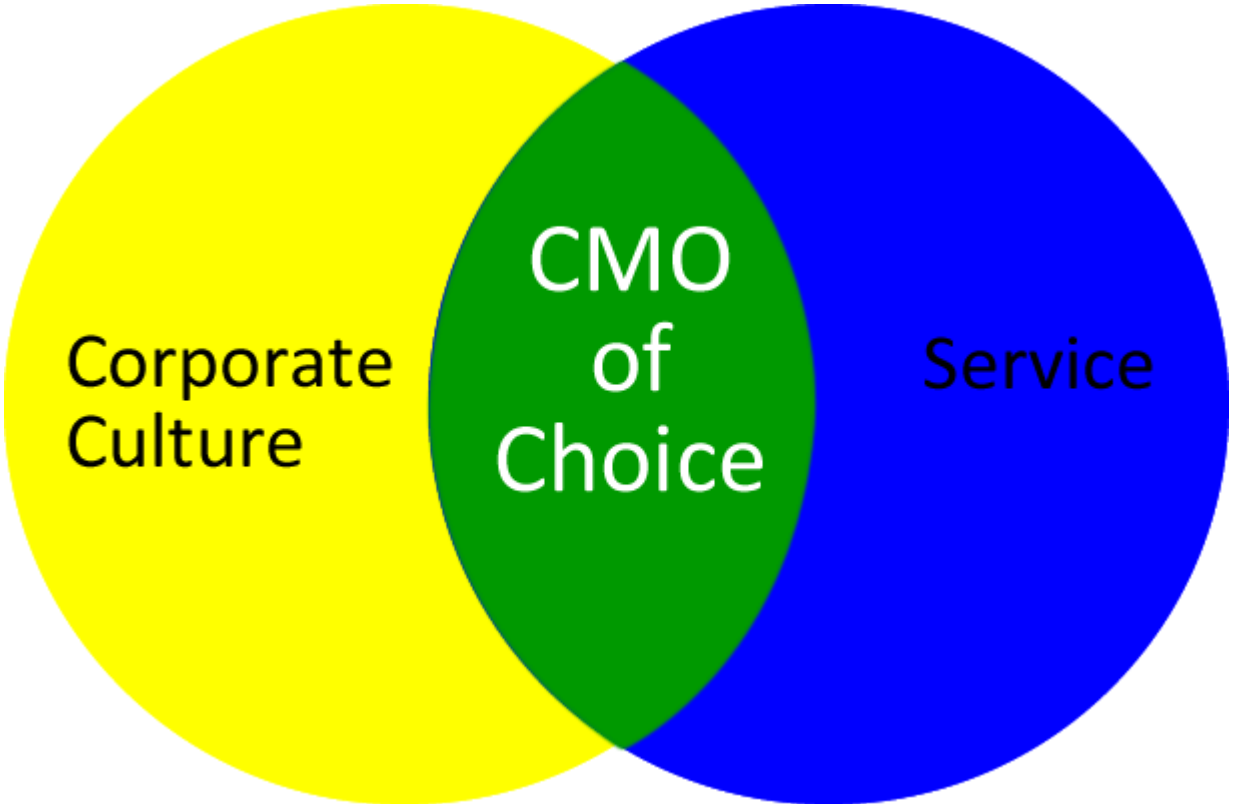
Attribute*	Move From Liquid Vial	Move From Lyo Vial
Container/Closure	Similar? Leverage previous extractable/leachable studies. Functionality: siliconization may be needed.	
Formulation	No change.	Change from freeze-dried powder to liquid.
Storage Conditions	No change. Stability Study: 3 months comparative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

* Indication and Administration Route changes need clinical data

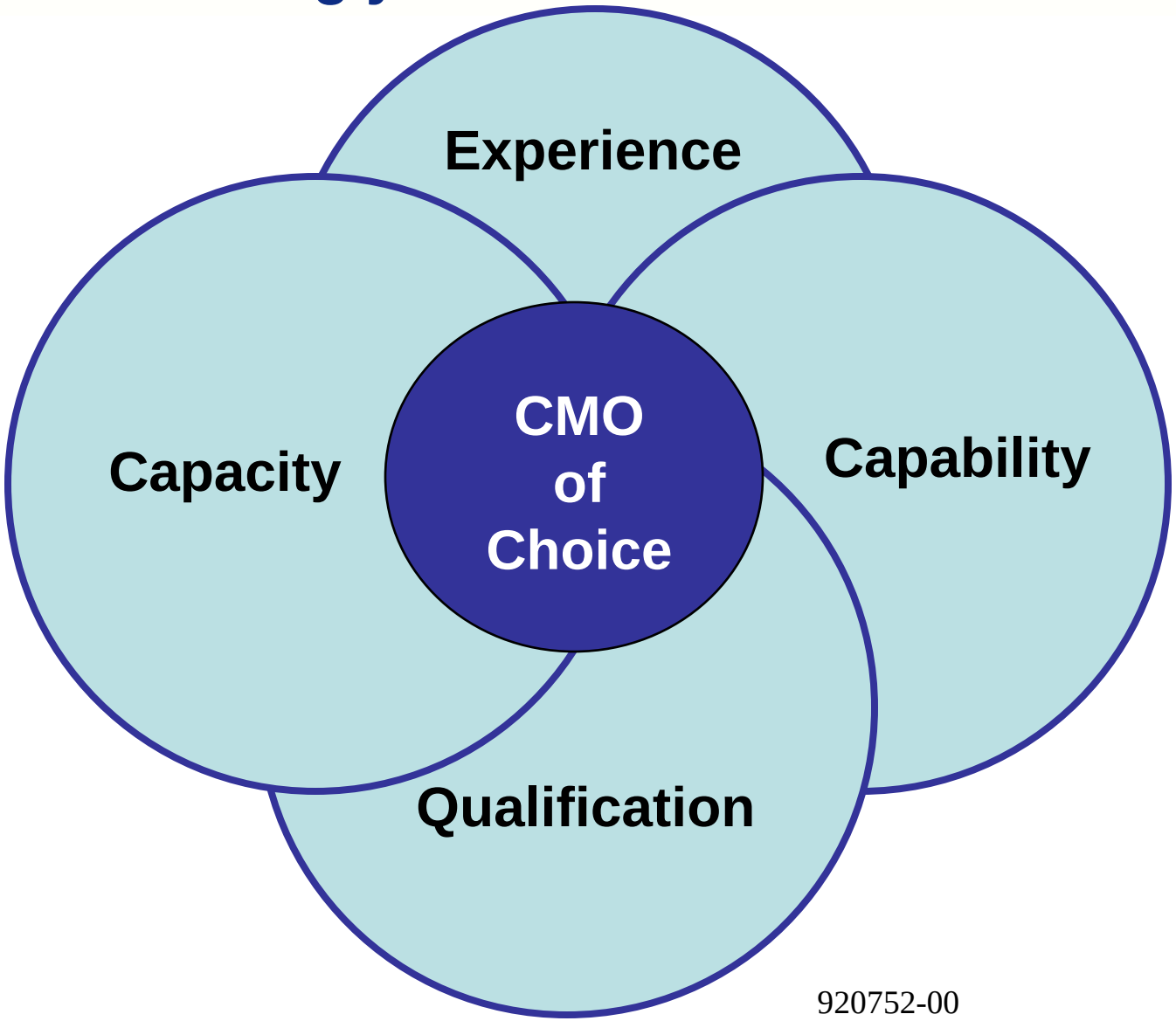
WHO?

CMO REQUIREMENTS

Who?



Who? Choosing your CMO . . .

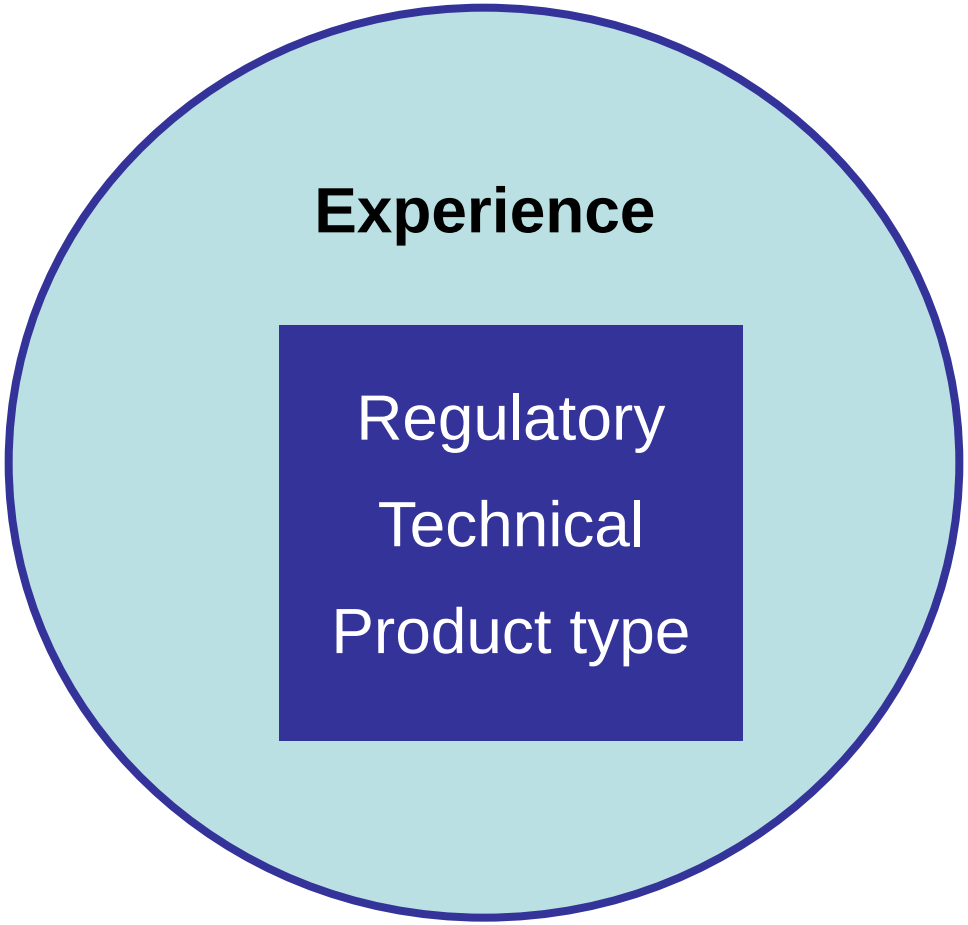


Experience

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

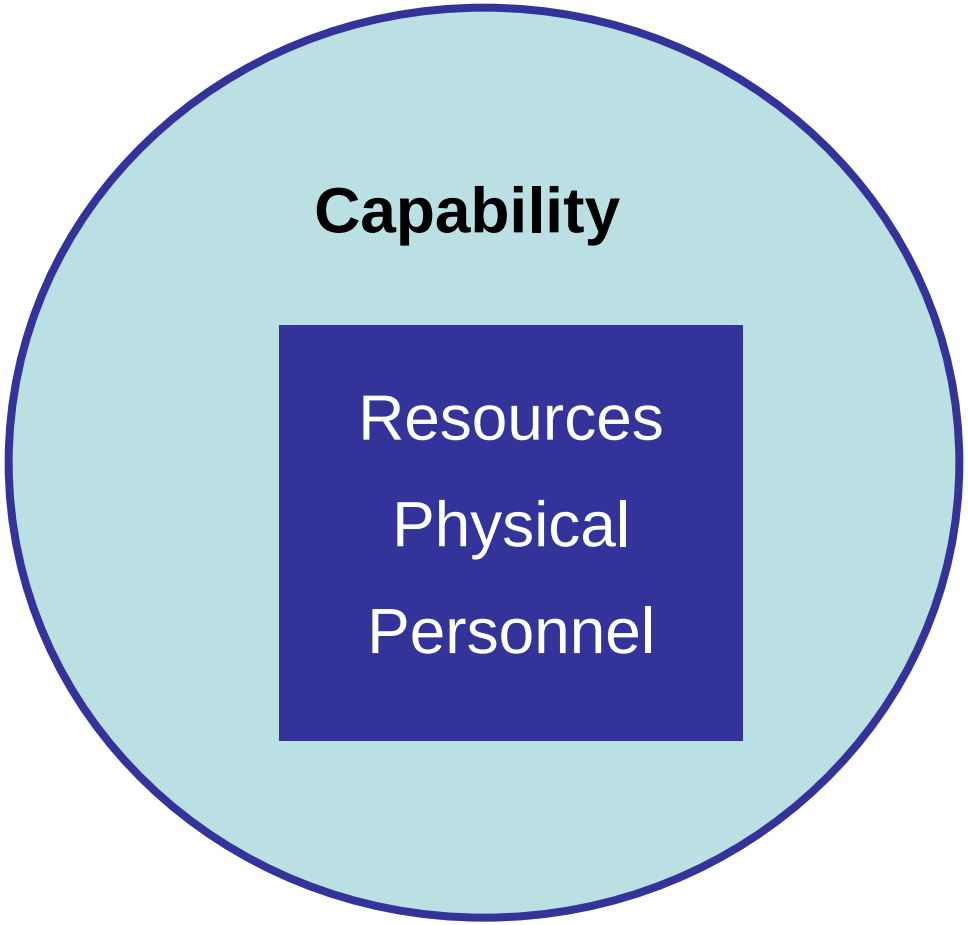


Capability

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

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

Personnel
- ✓ Education
- ✓ Training
- ✓ Experience

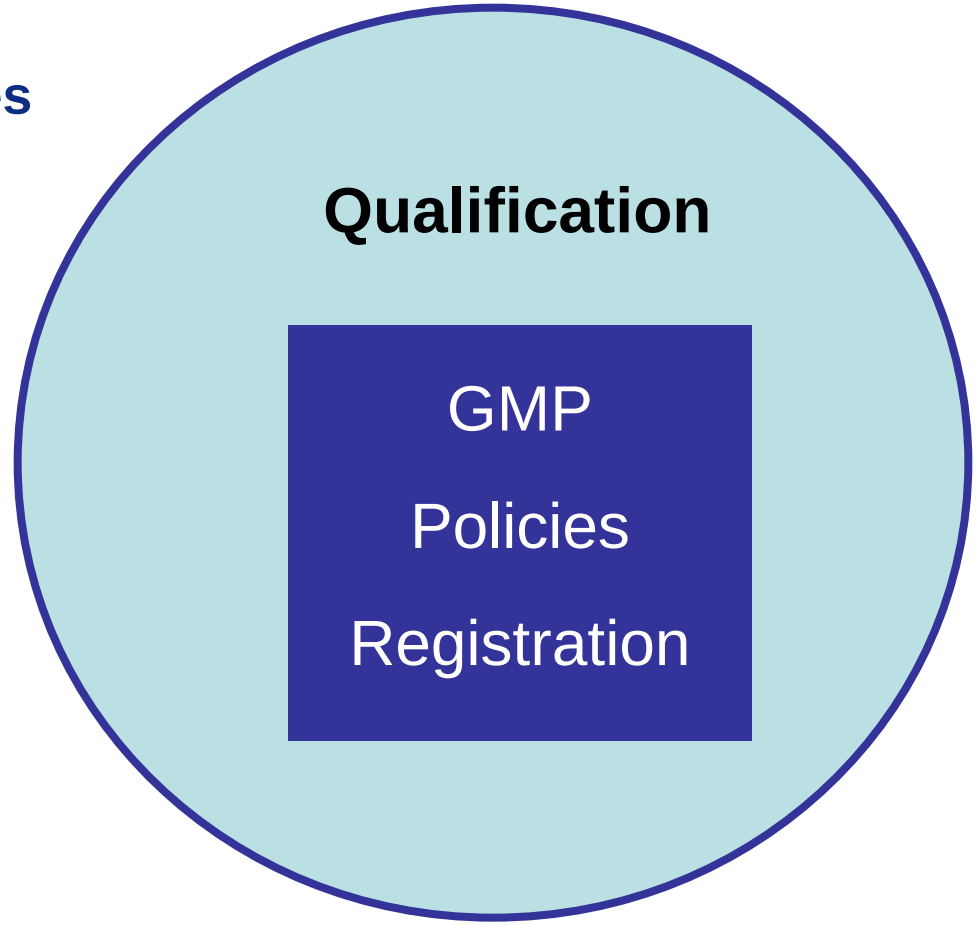


Qualification

Good Manufacturing Practices
- ✓ Compliance
- ✓ Documentation
- ✓ Training
- ✓ Audit

Company Policies
- ✓ Business
- ✓ Quality
- ✓ Regulatory
- ✓ Manufacturing

Registration
- ✓ National entities
- ✓ Regulatory Agencies

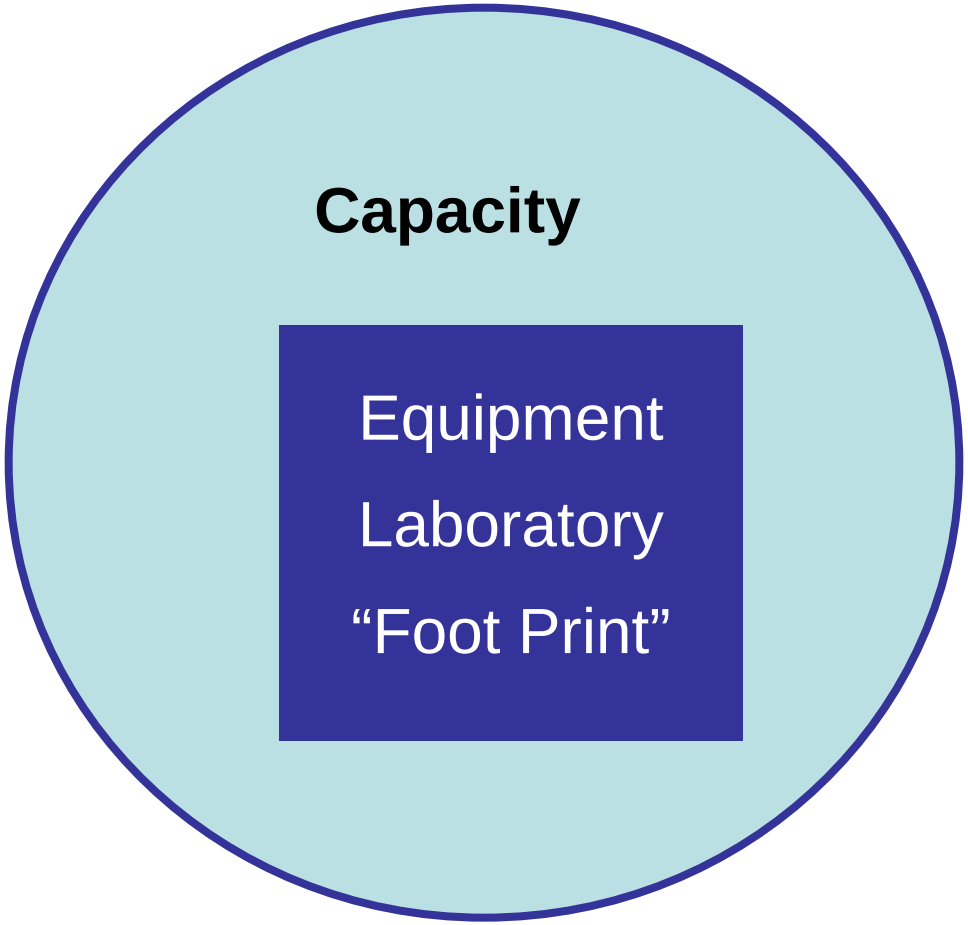


Capacity

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.

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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