

# All about Pre-filled Syringe Systems

From Initial Development to Final Fill Finish

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## Agenda – DAY 1

### **Overview and Introduction into the Pre-filled Syringe Market**

*Overview & Trends • Stakeholders • User's perspective*

### **Technical Aspects**

*Syringe • Plunger • Needle • Needle shield or Tip cap • Auto-injector •  
Regulatory guidelines and technical standards*

### **Overview & Introduction into Drug-Syringe Interactions**

*Aggregation • Degeneration • Oxidation • Viscosity • Bubbles*

### **Overview & Introduction to the Manufacturing Process of PFS**

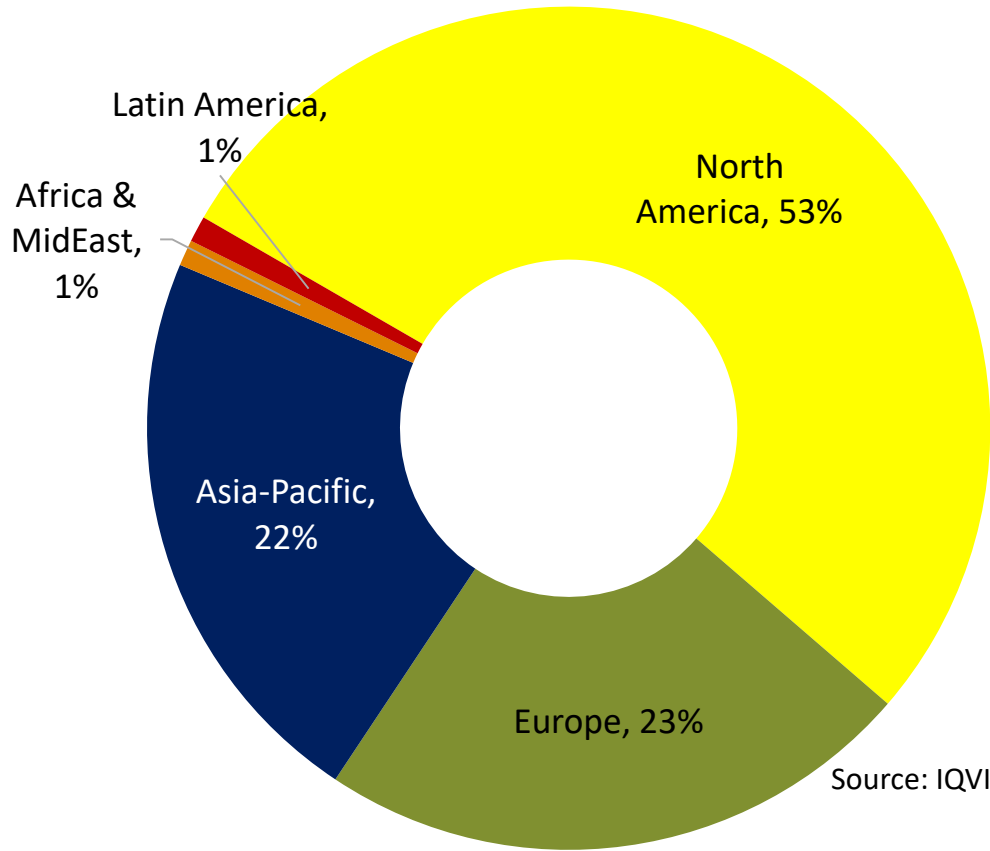
*Syringes Barrel Forming • Washing • Siliconization • Sterilization • Regulatory  
guidelines and technical standards ...*

### **Fill and Finish**

*Filling • Stoppering • Assembly • Technical Standards*

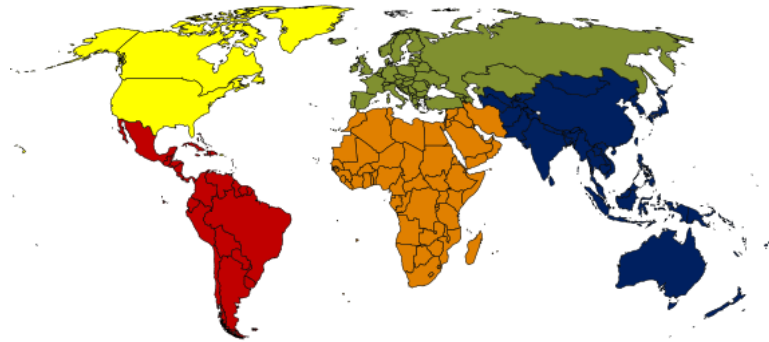
### **Hands-on Session 1**

# Injectable Value Share By Region



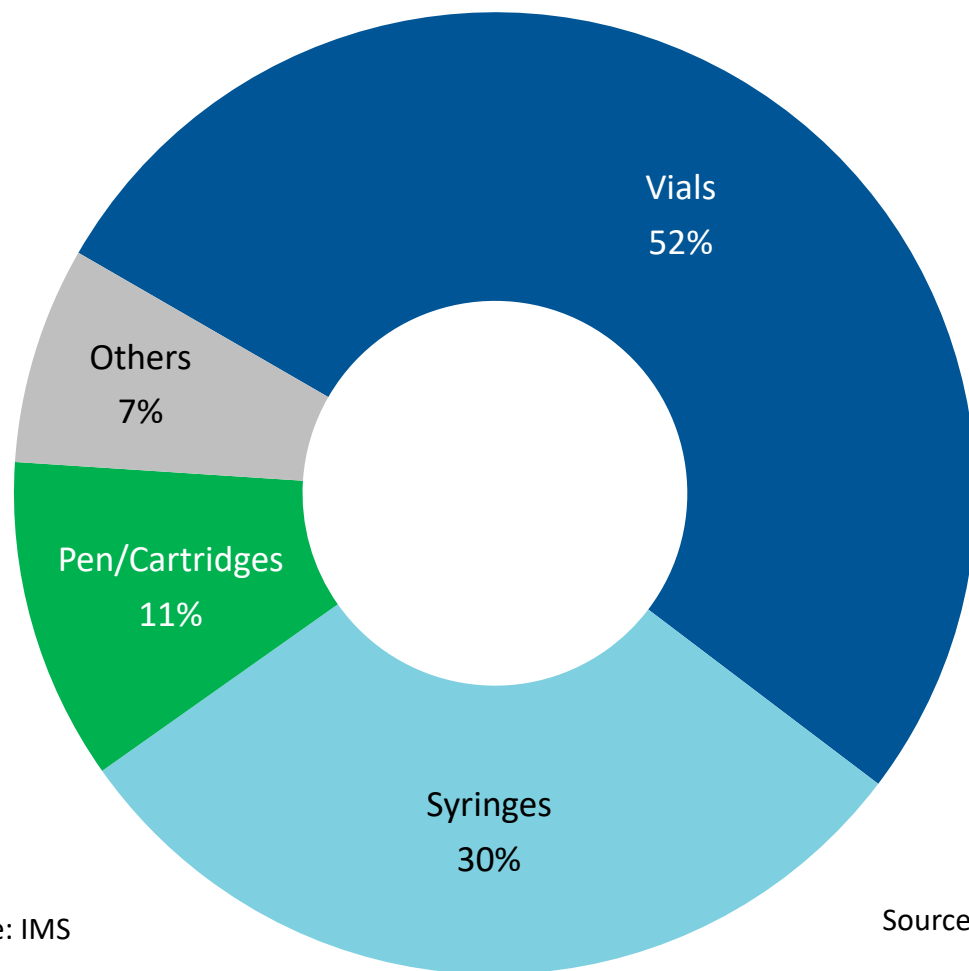
Source: IQVIA

Regions	'16 - '18 CAGR
Global	10%
North America	12%
Europe	11%
Asia-Pacific	3%
Africa & MidEast	14%
Latin America	-12%



As of 2018, North America is the largest market by value, while Asia is the largest market by volume

# Injectable Value Share By Format



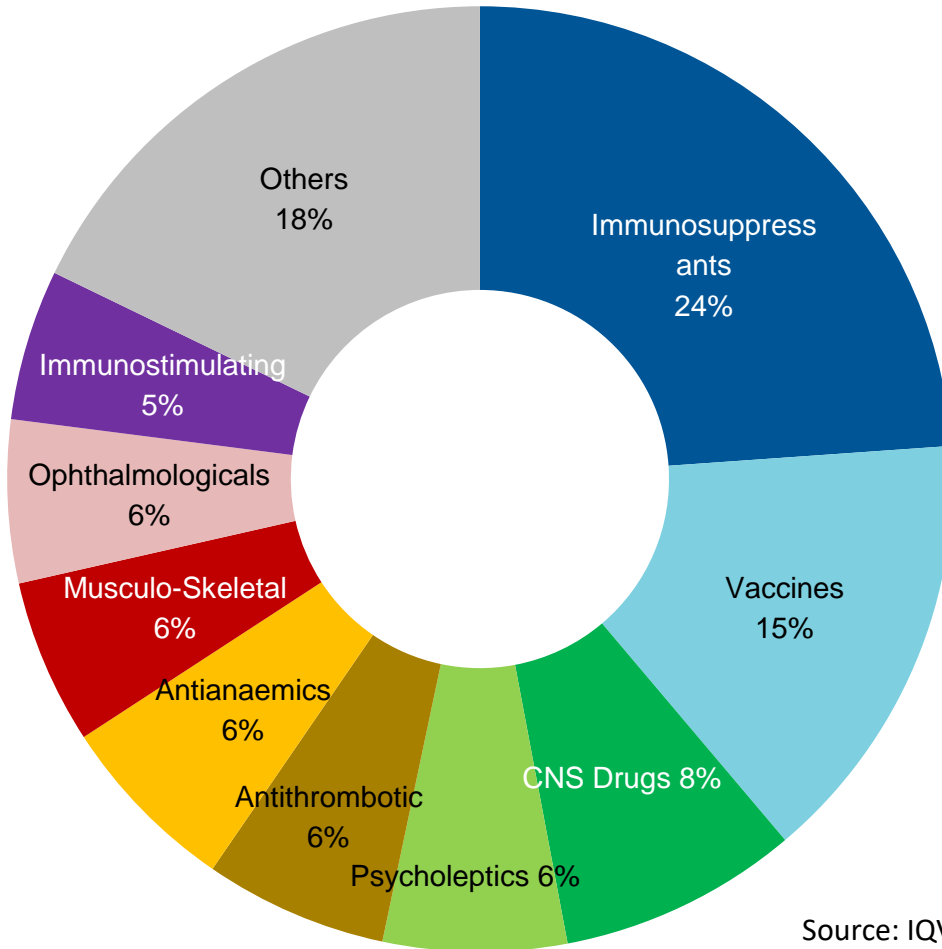
Source: IMS

Source: IQVIA

Regions	'16 - '18 CAGR
Vials	8%
Syringes <sup>1</sup>	15%
Pen/Cartridges	11%
Others <sup>2</sup>	0%
Total	10%

1. Includes PFS & Auto-injectors
2. Includes Ampoules, Implants, & Bags

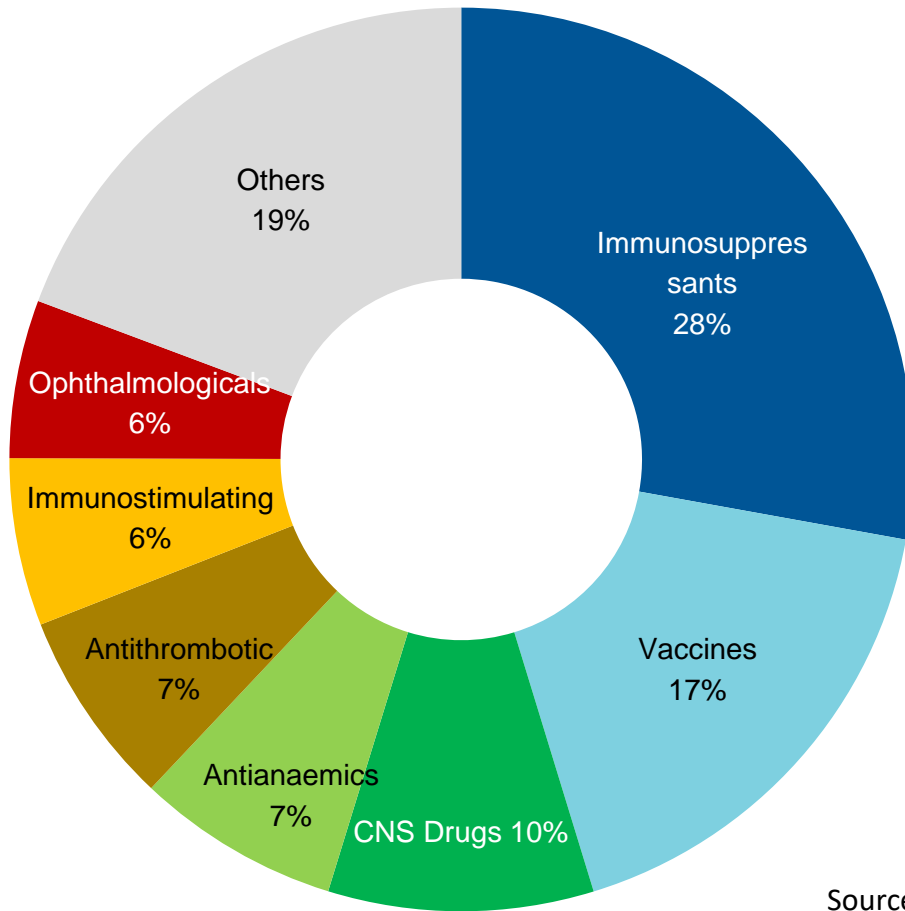
# 2018 Global PFS Value Market By Top Therapy Area



Regions	'16 - '18 CAGR
Immunosuppressants	15%
Vaccines	12%
CNS Drugs	-9%
Psycholeptics	25%
Antithrombotic Agents	-1%
Antianaemics	2%
Musculo-Skeletal	11%
Ophthalmologicals	43%
Immunostimulating	-9%
Total PFS Market	9%

Source: IQVIA

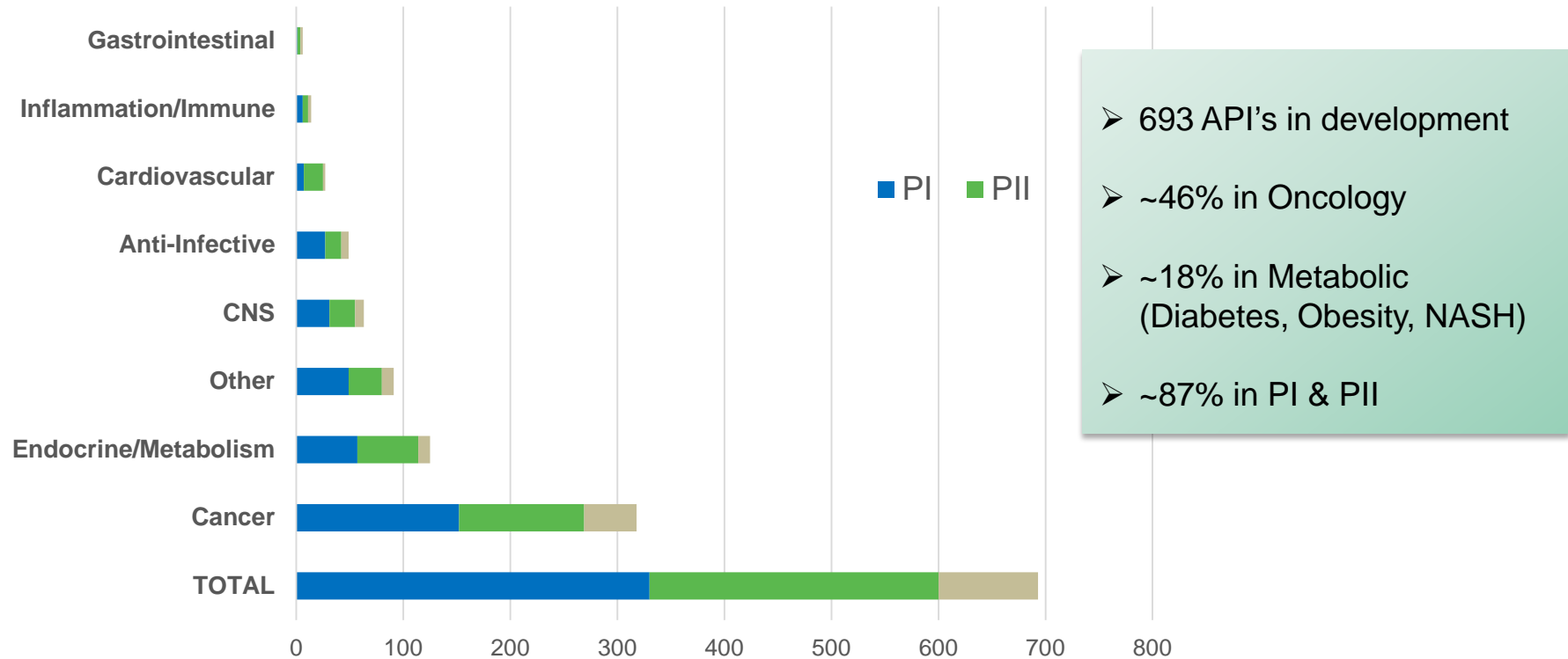
# 2018 Global Biologics PFS Value Market By Top Therapy Area



Regions	'16 - '18 CAGR
Immunosuppressants	14.8%
Vaccines	11.9%
CNS Drugs	-8.8%
Antianaemics	2.2%
Antithrombotic	-0.9%
Immunostimulating	-8.7%
Ophthalmologicals	51.4%
Total Bio PFS Market	8.8%

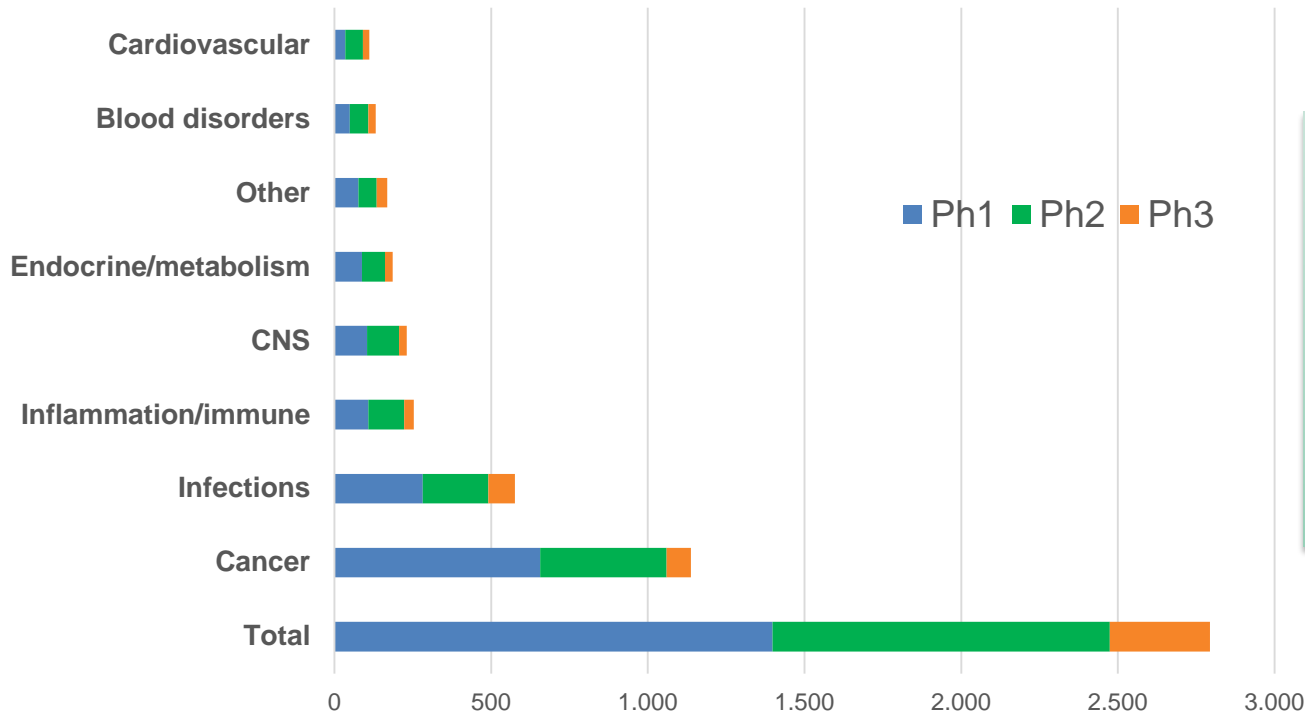
Source: IQVIA

# Injectables Small Molecule NME Pipeline



Source: PharmaCircle

# Injectable Biologics NME Pipeline



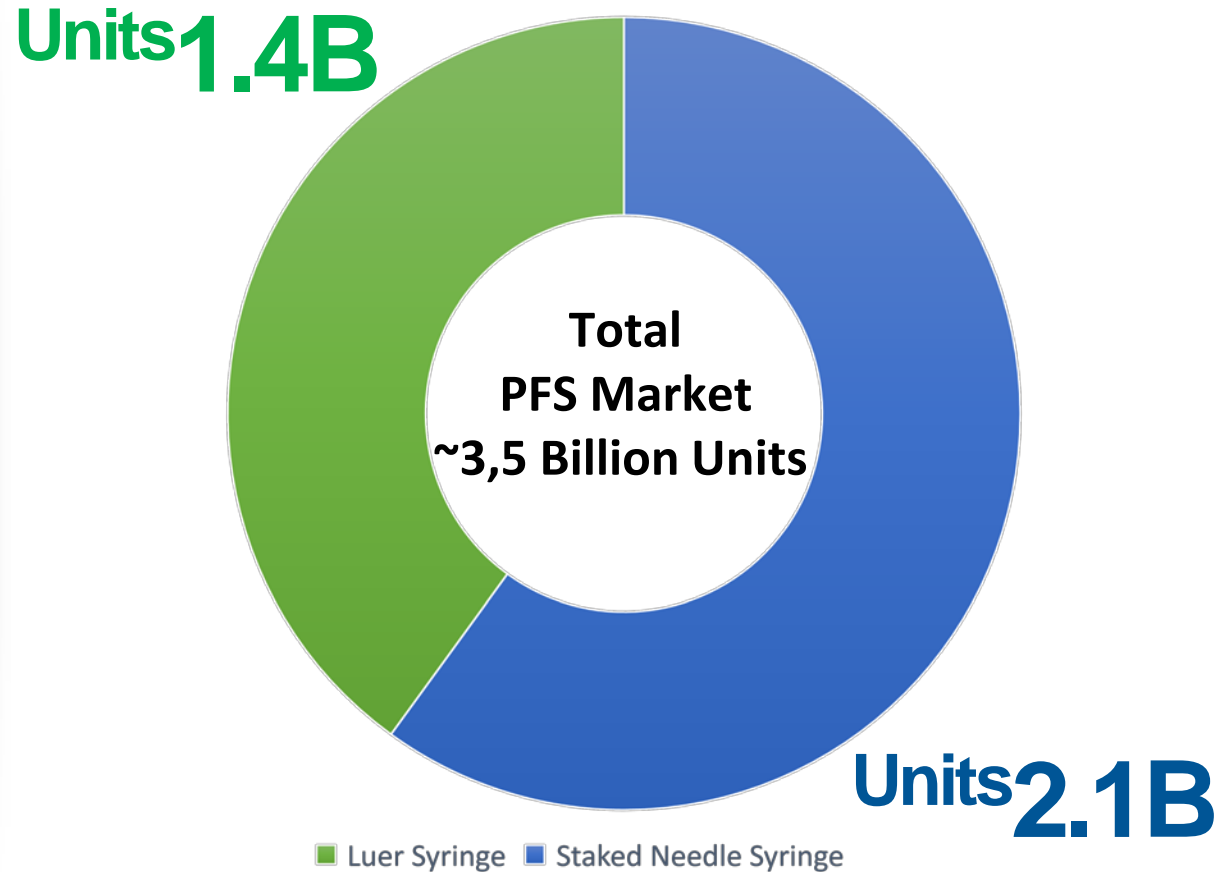
- 2794 API's in development
- ~41% in Oncology
- ~21% in Infections (vaccines)
- ~89% in PI & PII

Source: PharmaCircle



# Global Prefilled Syringe Luer vs Staked Needle

- The global prefilled syringe market is estimated to continuously grow at mid-single digit
- The majority of staked needle syringe applications use RNS



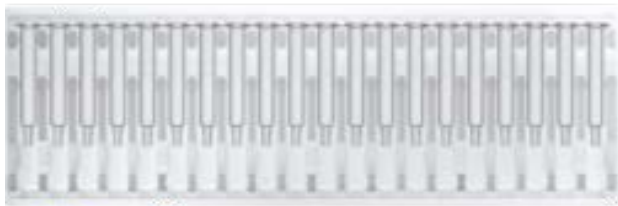
Data Source: best estimate, multiple sources

# Global Prefilled Syringe Bulk vs Ready-to-Use

Ready-to-Use  
Nested glass  
syringes in tubs

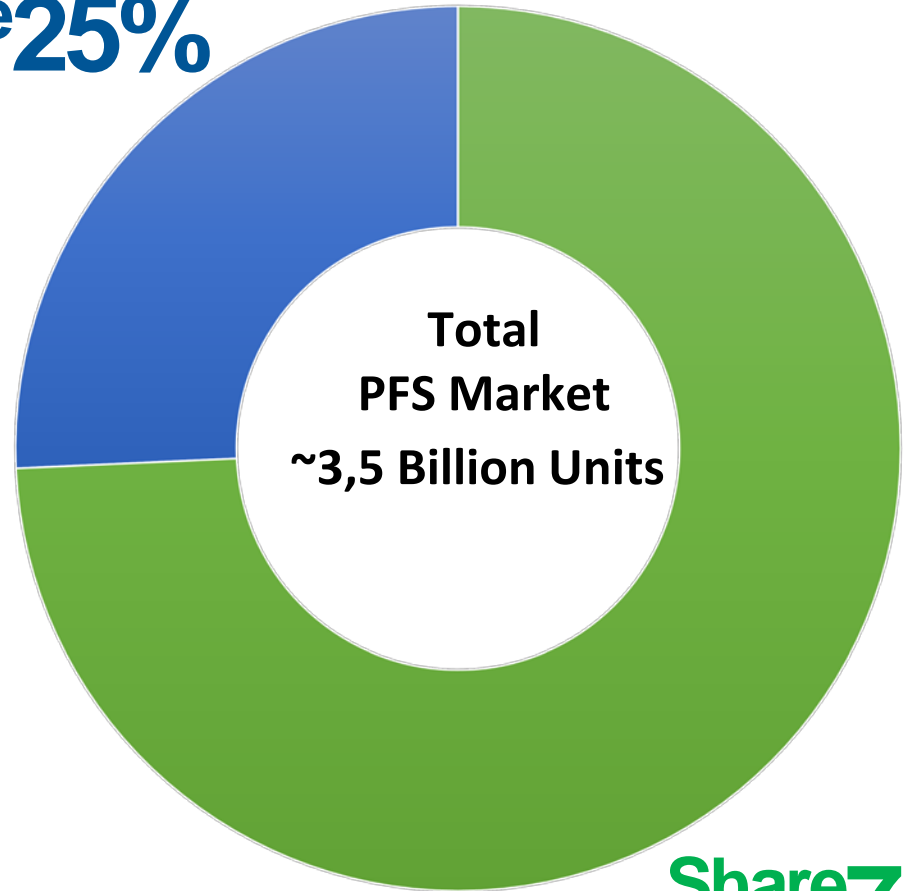


*Pictures property to Gerresheimer*



Bulk glass syringes on rondo trays

Share **25%**



**Total  
PFS Market  
~3,5 Billion Units**

■ nested syringes ■ bulk syringes

Share **75%**

**Increasing regulatory  
and cost pressure**

1

4

**Tech companies meet  
health companies**

**Specialty medicine  
as growth driver**

2

**Key Trends  
&  
Developments**

5

**High spending for  
non-communicable diseases**

**Maturing  
personalized medicine**

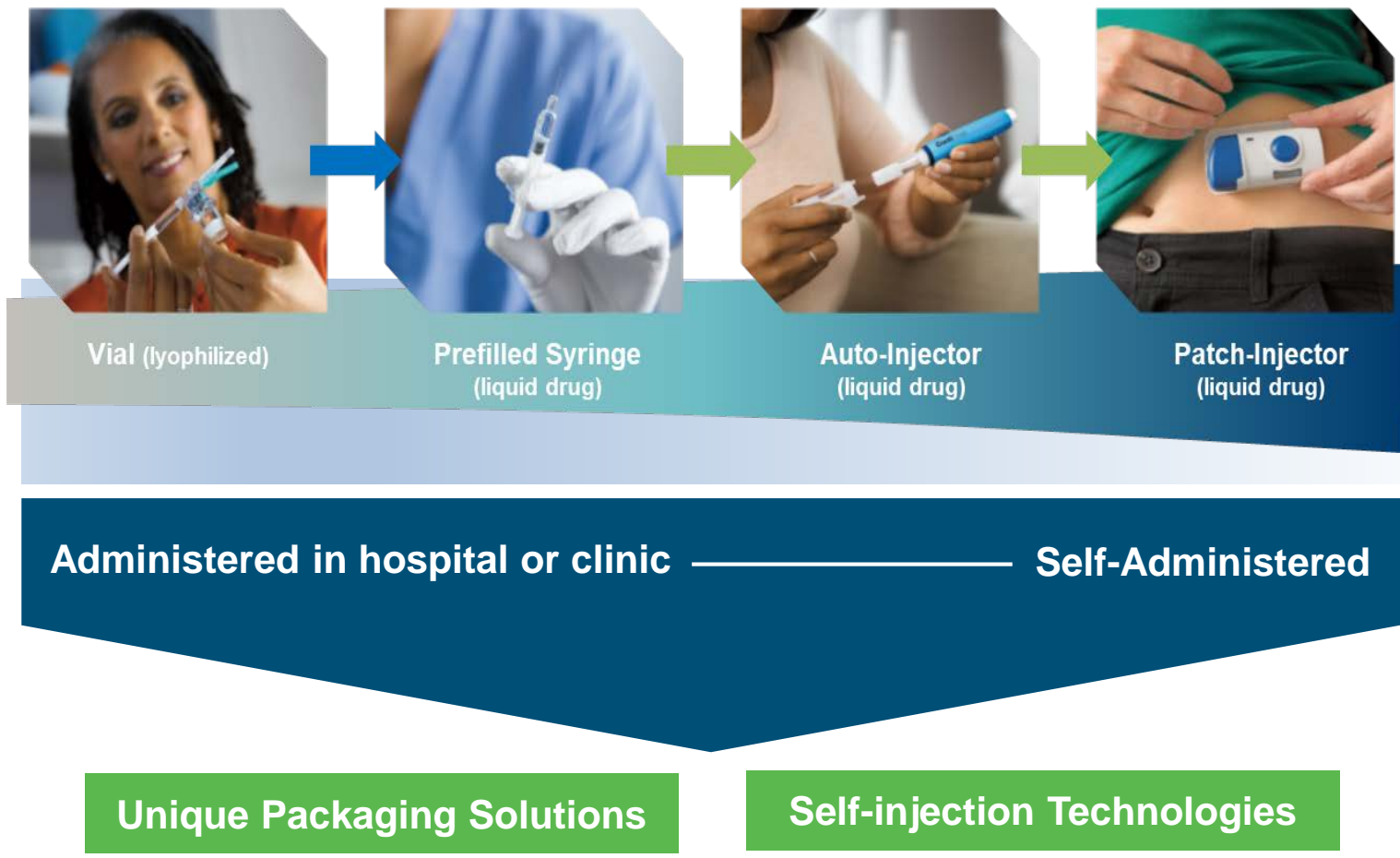
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**Big data and  
mobile health**

# What Does it Mean for Drug Administration?

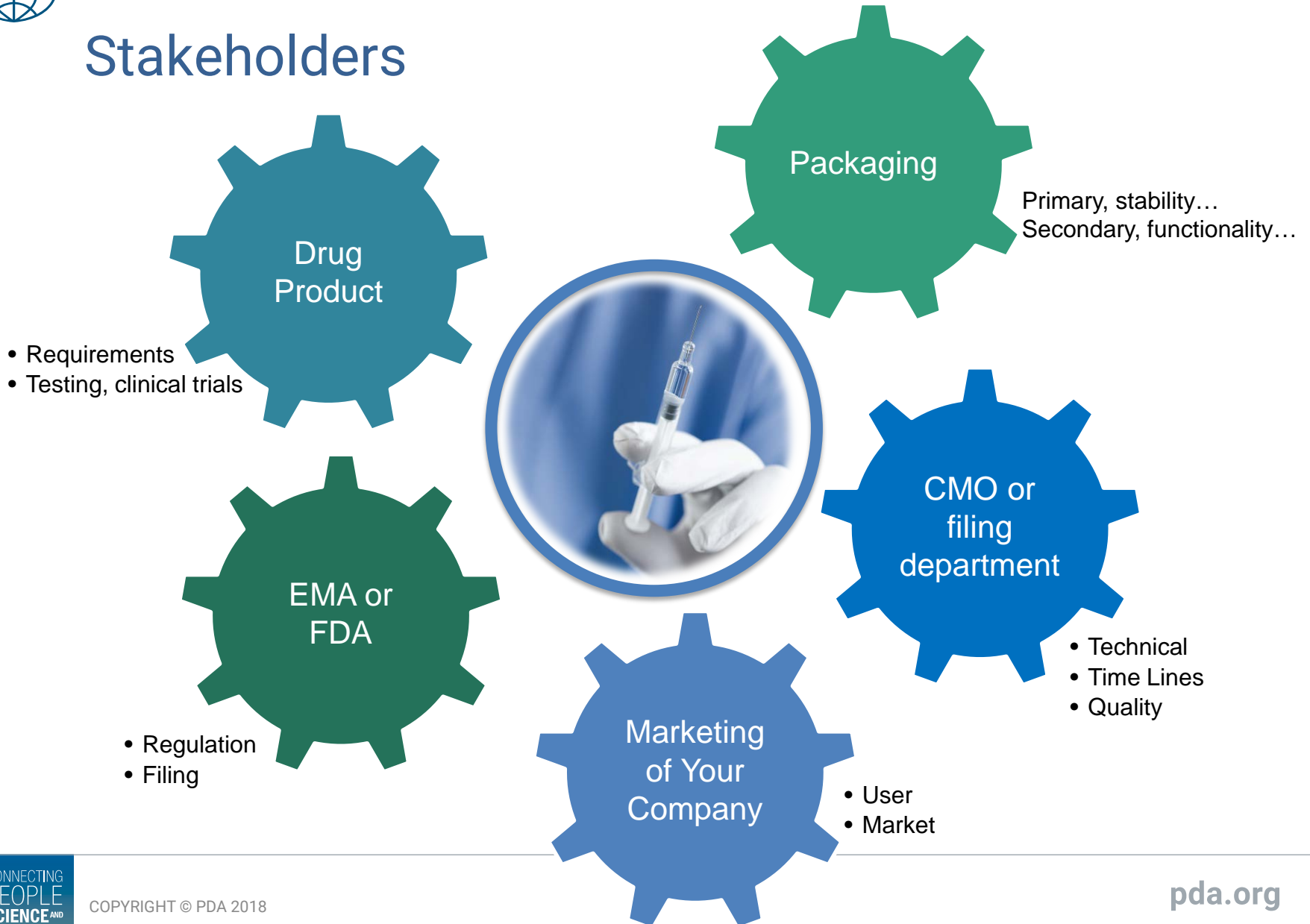
- More chronic diseases
- Homecare administration
- Patient compliance
- Digitalized application solutions



# Diverse Syringes for Diverging Needs

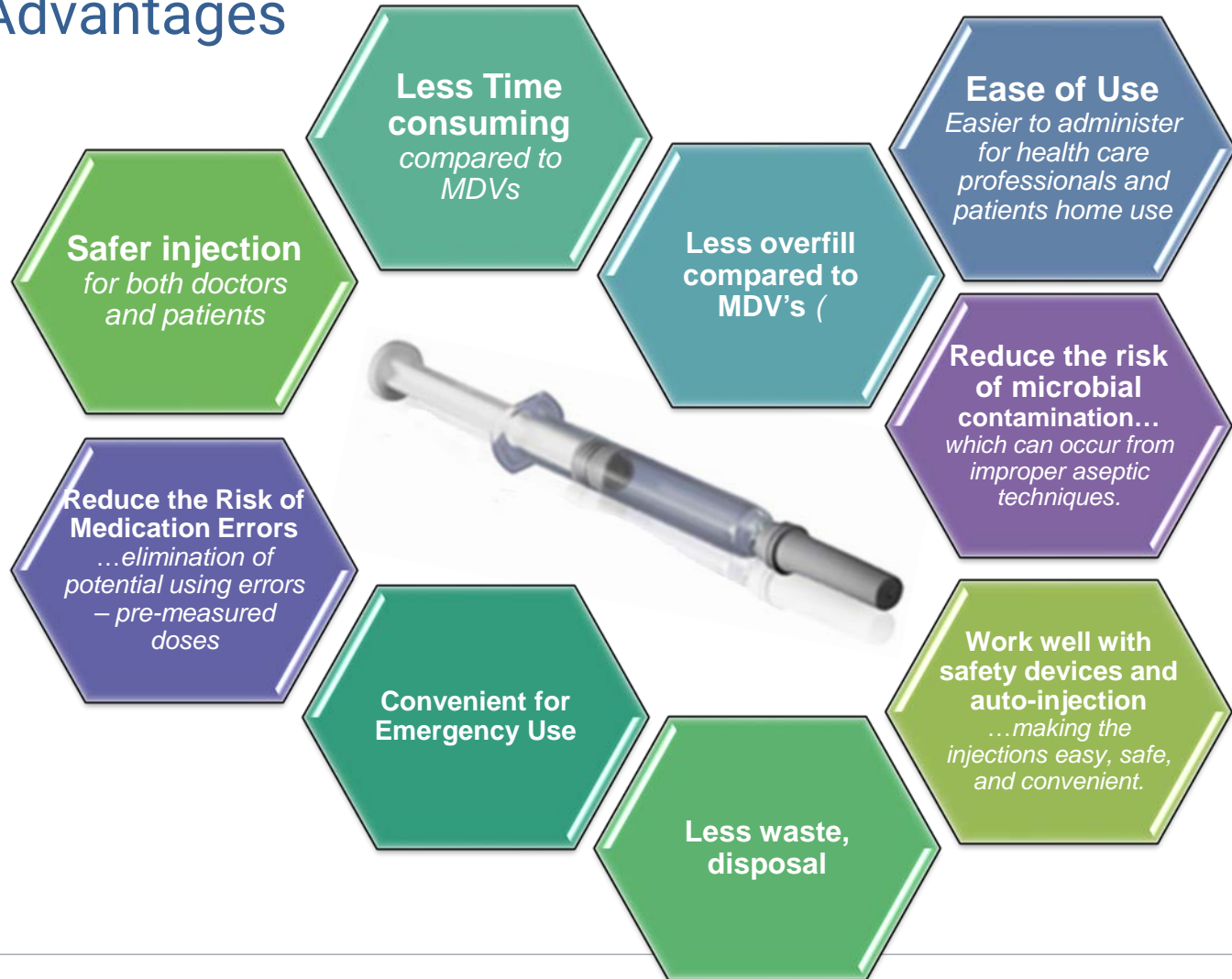
	Heparins - anticoagulants	Vaccines – mainly flu vaccines	Biotech – very diverse group	Aesthetics – beauty and lifestyle
Injection mode	Subcutaneous injection, 1/2” needle	Intramuscular injection, 5/8” needle	Subcutaneous injection, 1/2” needle	Subcutaneous injection, diverse needles SC
Syringe format	0,5 mL and 1 mL long with staked-in needle	1 mL short → trend towards Luer Lock	1 mL long 2.25 mL ...	Luer Lock 1 mL Long
Batch size	High volume	High volume	Small batch Sizes	Mid batch Size
Device application	Safety device integration	Back Stop	Auto Injector use	Possible
Very high focus on	Processability & speed	Processability & speed	Sensitive drugs, often small fill lines	Appearance
Price sensitiveness	+++	+++	+	+
Remarks	Few players, mass market	Few players, mass market	Specialty: Ophthalmics: luer lock, dose mark, particles	Hyaluronic acid not oxygen sensitive

# Stakeholders



# Multi Dose Vials MDV's - Prefilled Syringes

## Some Advantages

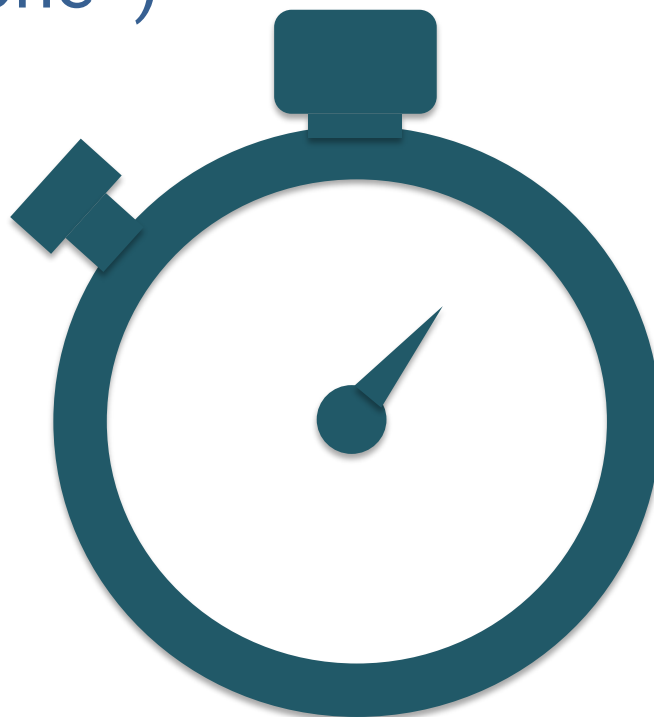


# Convenience / Ease of Use / Patient Satisfaction (e.g. Copaxone<sup>®</sup>)



Preparing injection for  
COPAXONE<sup>®</sup> filled in a vial

**235 sec.**



Preparing injection for  
COPAXONE<sup>®</sup> filled in PFS

**38 sec.**

A typical patient is able to save about **20h a year** by using  
Copaxone<sup>®</sup> in a PFS format

*Copaxone<sup>®</sup> is a registered trademark of Teva Pharmaceutical Industries Ltd.*



# Administration Speed

## Steps to prepare Lyophilizate for Injection: the “old way”

- 1 • Take empty syringe
- 2 • Attach cannula
- 3 • Draw WFI from vial into syringe
- 4 • Change cannula
- 5 • Pierce lyo stopper & insert water into lyo vial
- 6 • Dissolve lyophilizate
- 7 • Take new syringe and attach cannula
- 8 • Draw drug into syringe
- 9 • Attach injection cannula onto syringe
- 10 • Inject drug into patient

## Steps to prepare Lyophilizate for Injection: the “optimized way”

- 1 • Open syringe and screw it onto the vial adapter
- 2 • Pierce lyo vial with vial adapter, transfer WFI into syringe
- 3 • Dissolve lyo product
- 4 • Invert vial & withdraw drug into the same syringe
- 5 • Disconnect syringe from vial adapter, attach injection cannula
- 6 • Inject drug into patient



# User and Payer

**User: Health care worker or patient**

**Payer: Health system or self payment**

Home use or hospital use



Cost pressure towards self use

Convenience, safety



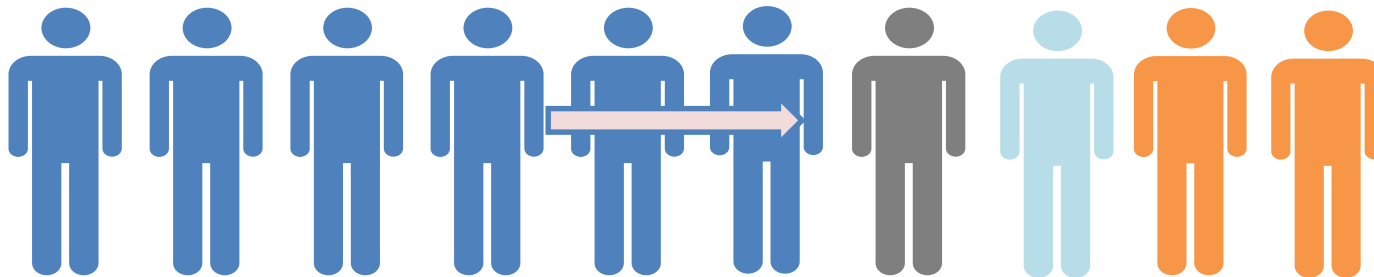
Vial vs. Prefilled Syringe, Safety Syringe, Auto-injector, Wearable

70%

<<10%

10%

20%



**Infusion – vial or bottle**

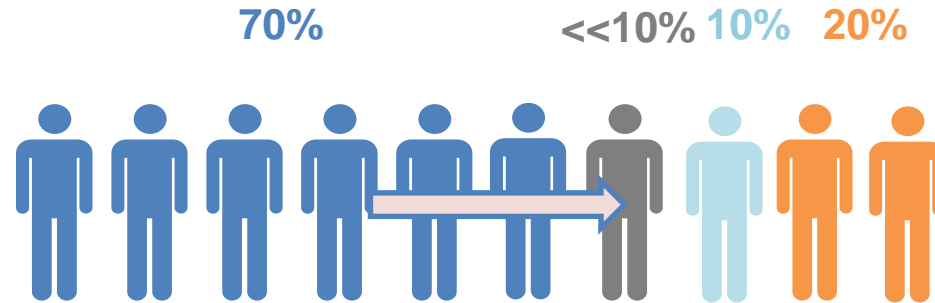
**Wearable – vial or cartridge inside**

**Auto-injector – syringe inside**

**Safety syringe**

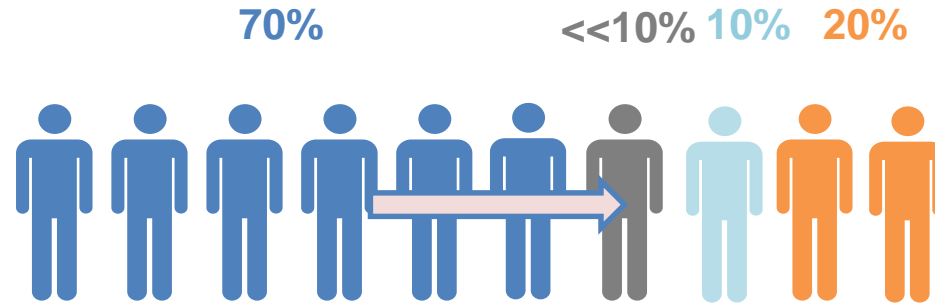
**Prefilled Syringe**

# User's perspective



	Infusion – vial or bottle	Wearable – vial or cartridge inside	Auto-injector – syringe inside	Safety syringe	Prefilled Syringe
<b>Hospital use or doctor's office</b>					
<b>Home use</b>					
<b>Injection time</b>					
<b>Cost of device</b>					
<b>Cost for health system</b>					
<b>e.g.</b>					

# User's perspective



	Infusion – vial or bottle	Wearable – vial or cartridge inside	Auto-injector – syringe inside	Safety syringe	Prefilled Syringe
<b>Hospital use or doctor's office</b>	main use	no	rare	yes	frequent
<b>Home use</b>	rare	convenient	convenient	yes	yes
<b>Injection time</b>	🕒🕒🕒🕒🕒	🕒🕒	🕒	🕒	🕒
<b>Cost of device</b>	\$	\$\$\$\$\$	\$\$\$\$	\$\$\$	\$\$
<b>Cost for health system</b>	\$\$\$\$\$	\$\$\$\$	\$\$\$	\$\$	\$
<b>e.g.</b>	Cancer treatment	Autoimmune disease	Autoimmune disease	Anticoagulants - Heparin	Vaccine

# Requirements towards containers Pharmacists perspective



# Requirements towards Injections and Ophthalmic

## FDA Guidance Container Closure Systems for Packaging Human Drugs and Biologics

- Packaging Description is part of the Registration Dossier
- Material in direct contact to the dosage form
- Storage/stability - transport - functionality (prefilled syringe is a device)
- Standards help all stakeholders

### Protection

- ✓ Temperature
- ✓ Light
- ✓ Water loss
- ✓ Loss of solvent
- ✓ Oxygen
- ✓ Microbial ingress

### Compatibility

- ✓ Adsorption
- ✓ pH change
- ✓ Precipitation
- ✓ Colour change
- ✓ Packaging brittleness

### Safety

- ✓ Leachables
- ✓ Extractables
- ✓ Toxicity
- ✓ Glue or ink migration
- ✓ Breakage, drop test

### Performance

- ✓ CCI
- ✓ Drug delivery
- ✓ NS pull off
- ✓ Break loose and gliding
- ✓ Usability: elderly people, children
- ✓ Connections