

# All about Pre-filled Syringe Systems

From Initial Development to Final Fill Finish

## The Pre-filled Syringe Market

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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**

# What type of containers are used for injectables?

## Prefilled Syringes



- › Elastomeric Components:
- › Plungers, Tip Caps and [Rigid] Needle Shields



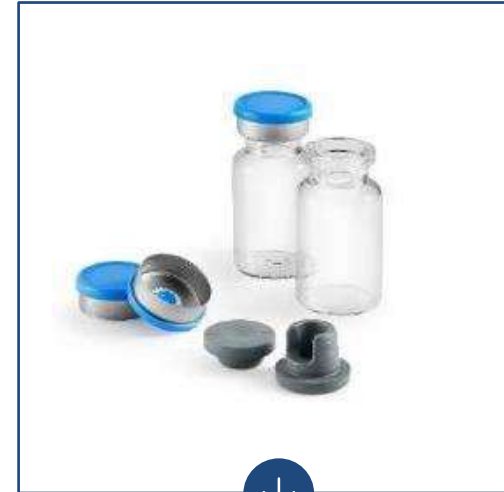
## Cartridges



- › Elastomeric Components:
- › Plungers Lined Seals



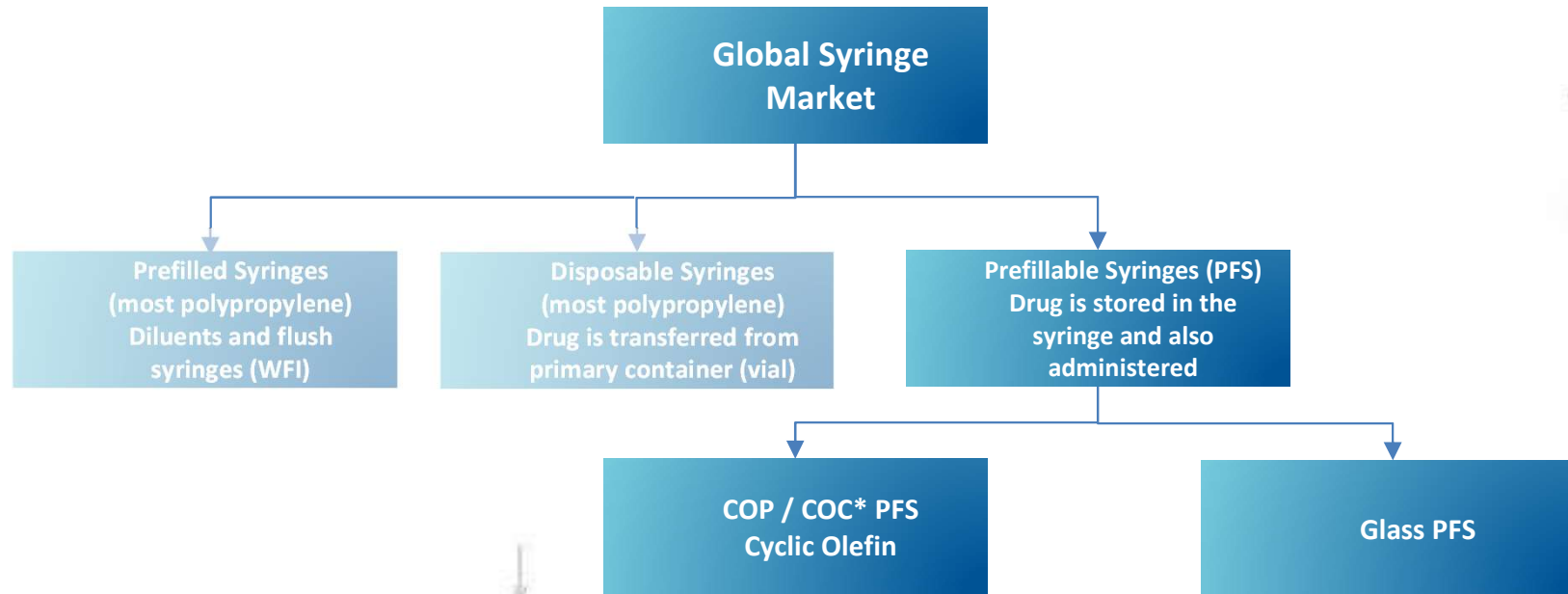
## Vials



- › Elastomeric Components:
- › Lyophilization or Serum Stoppers

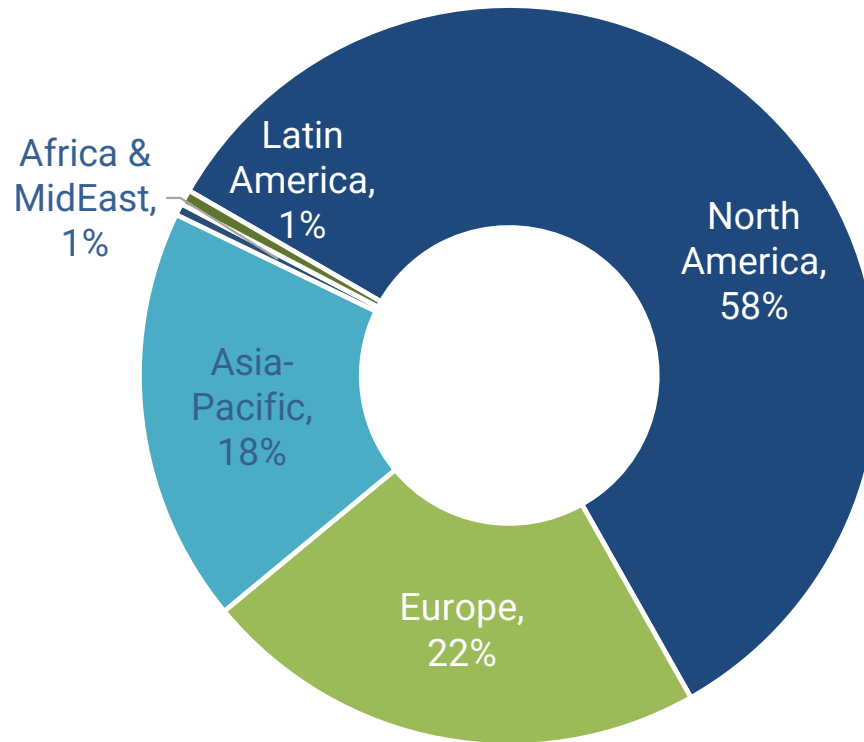


# Syringe Market Overview



\* COP: Cyclic Olefine Polymer - COC: Cyclic Olefine Copolymer

## Injectable Value Share By Region, 2022

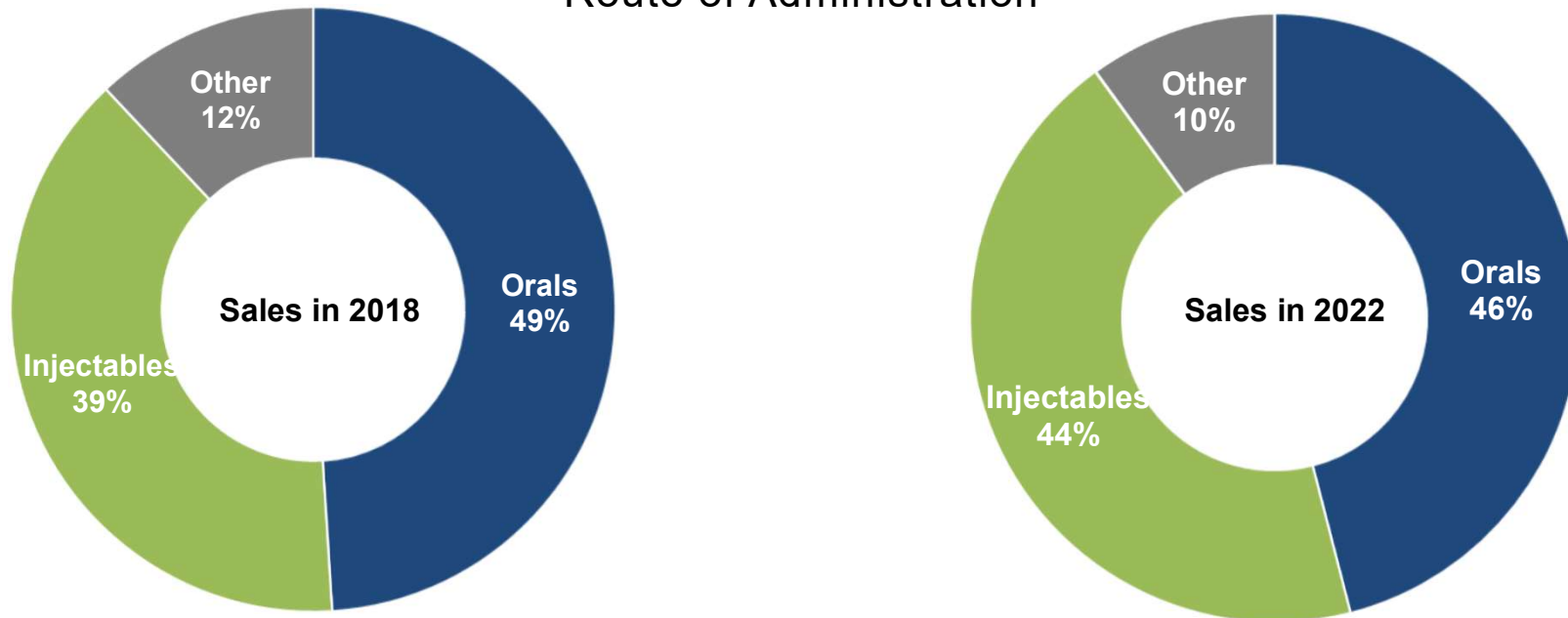


Regions	2018 - 22 CAGR
Global	9%
North America	11%
Europe	7%
Asia-Pacific	4%
Africa & MidEast	8%
Latin America	11%

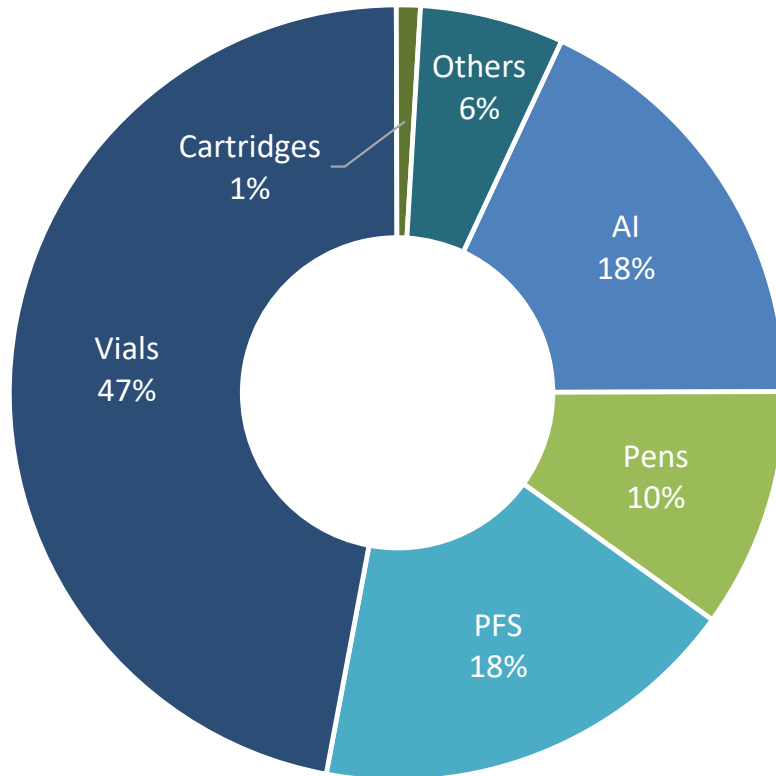
As of 2022, North America is the largest market by value, while Asia is the largest market by volume

## Share of Injectables is expected to increase through 2022

Global Market Share% by Route of Administration

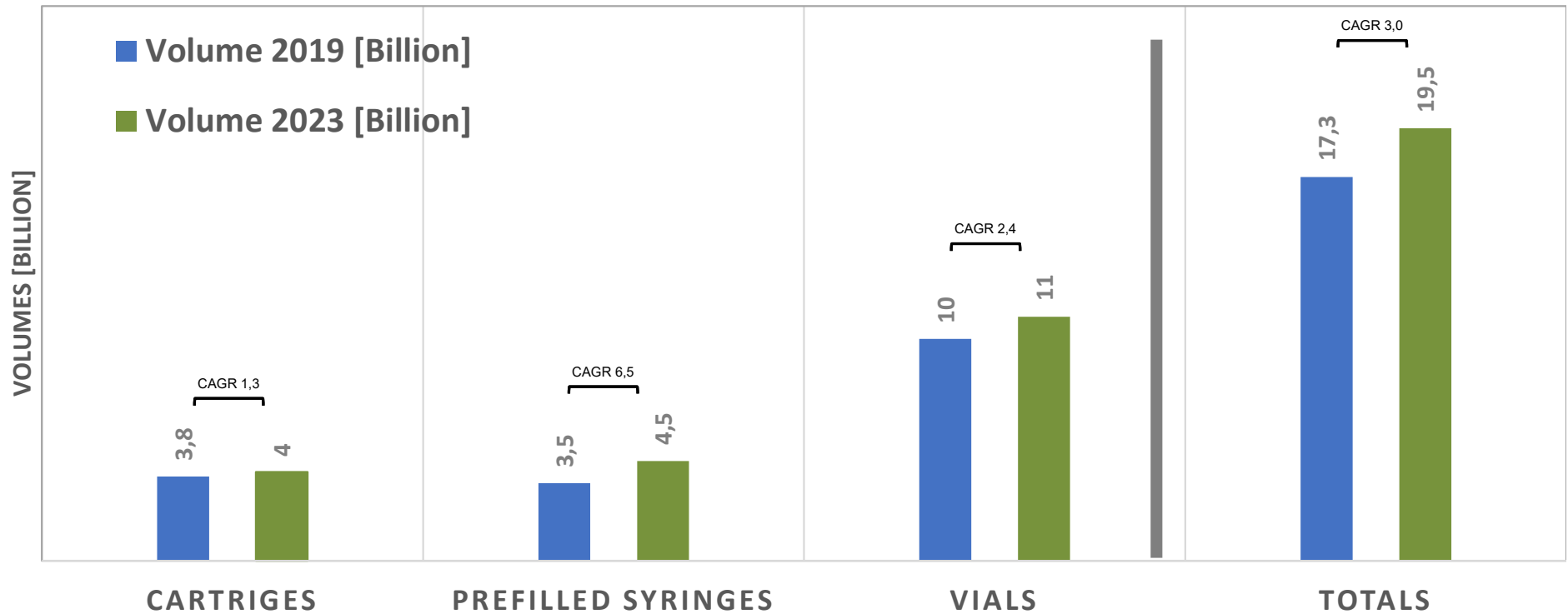


## Global Injectable Value Share By Format, 2022



Formats	2018 - 22 CAGR
AI	20%
Pens	11%
PFS	9%
Vials	6%
Cartridges	1%
Other injectables	2%
<b>Grand Total</b>	<b>9%</b>

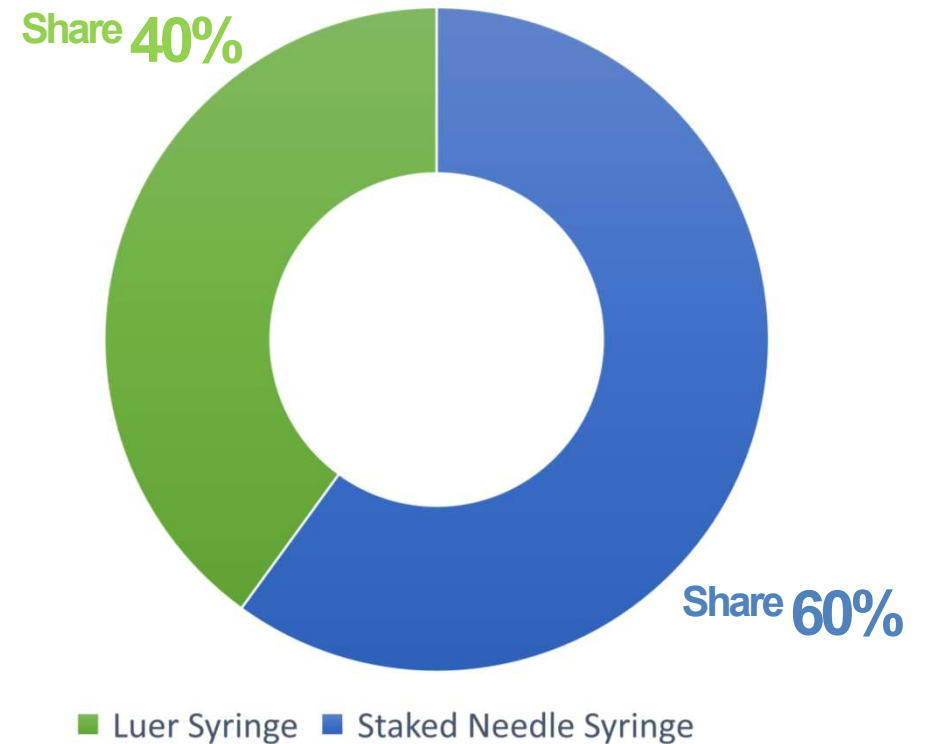
## Global Market for Parenteral Containers using Tubular Glass in Volume





## Global Prefilled Syringe Luer vs Staked Needle

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



## Global Prefilled Syringe Luer vs Staked Needle

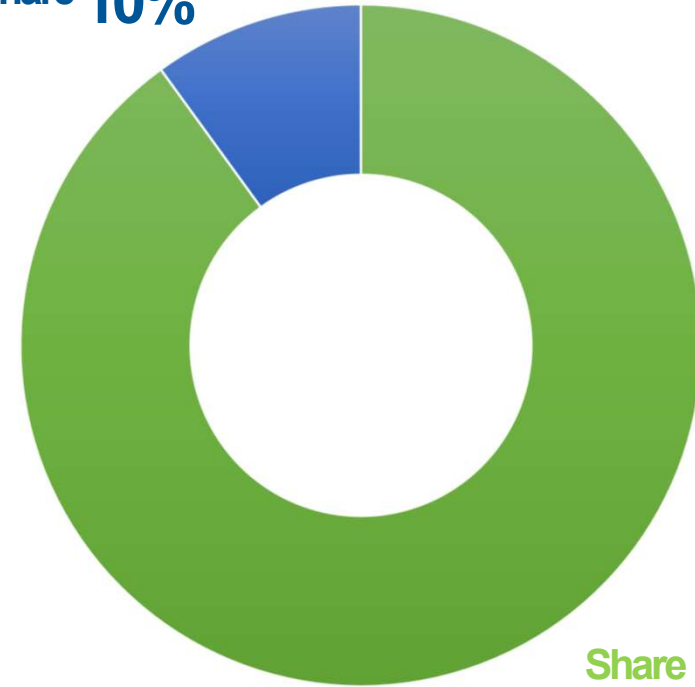
> Ready-to-Use Nested glass syringes in tubs



> Bulk glass syringes on rondo trays



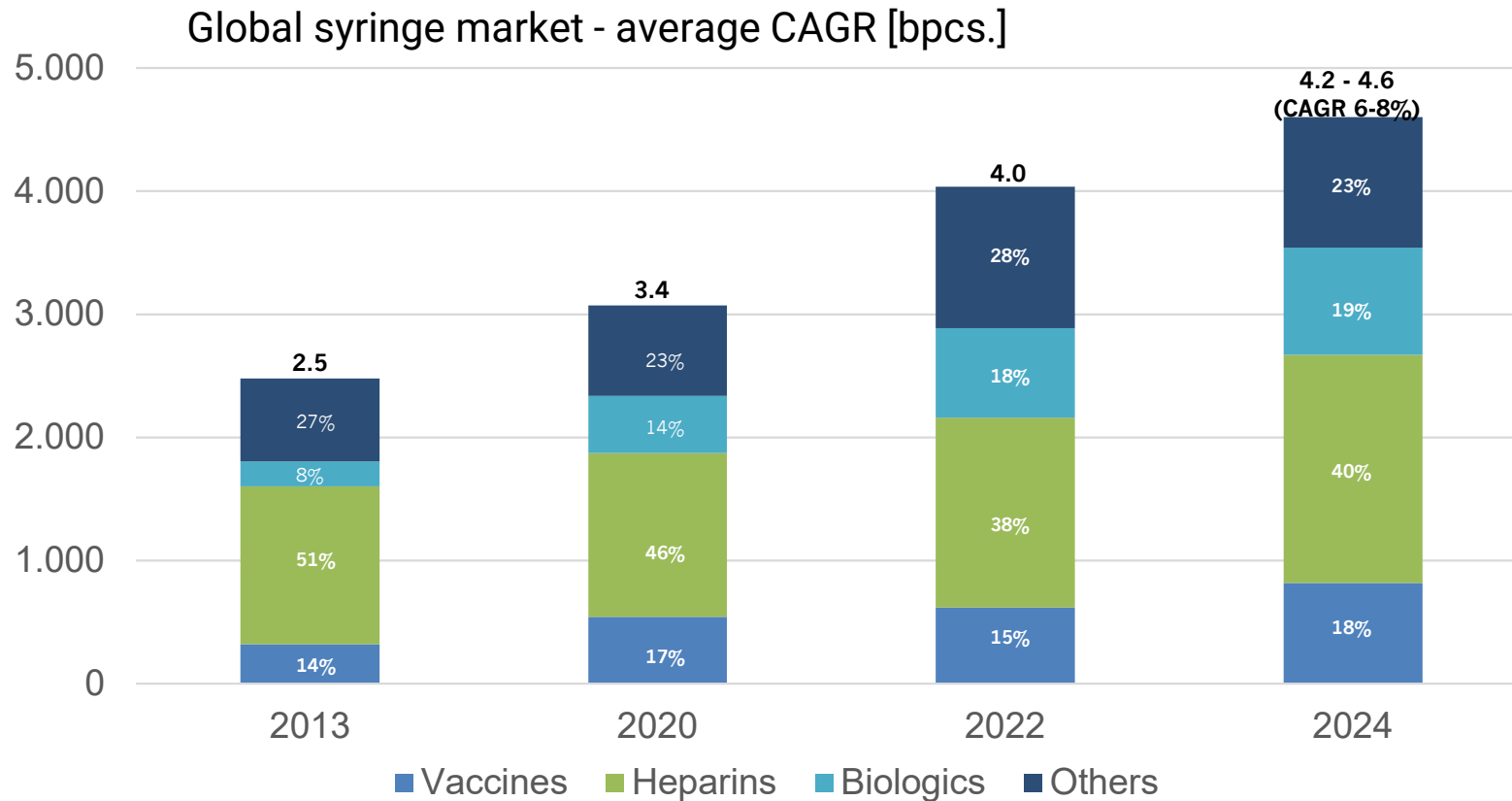
Share 10%



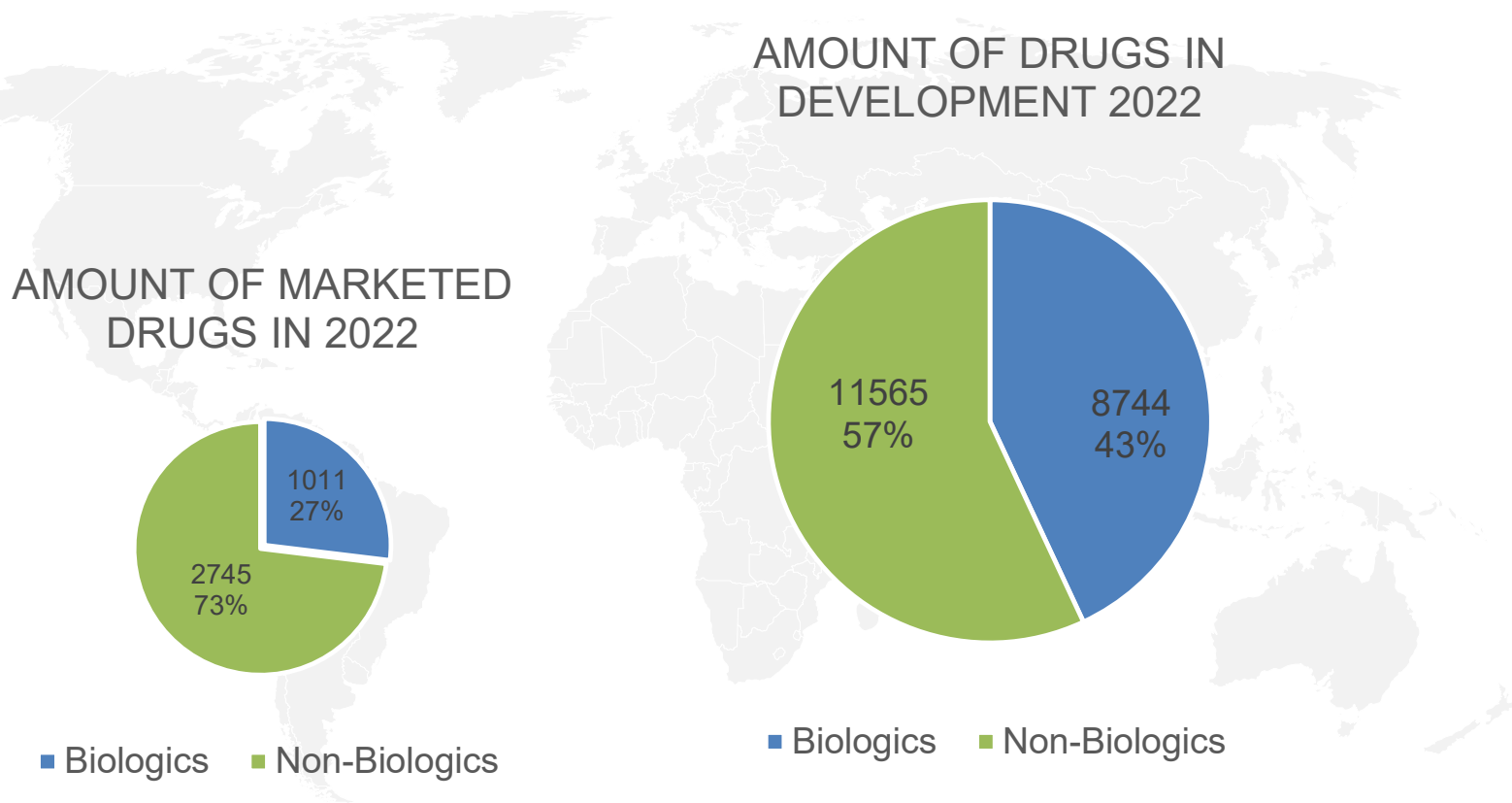
Share 90%

■ nested syringes ■ bulk syringes

# Syringe market demand per indication



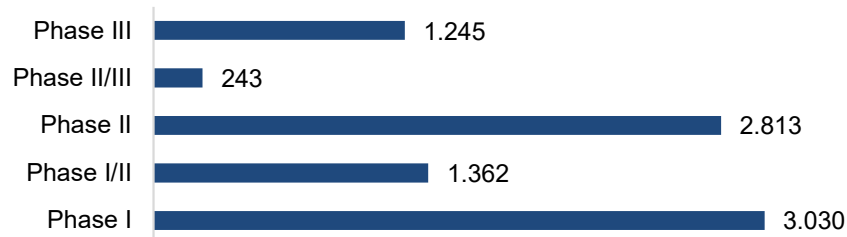
## Biologic / Non-Biologic market total in 2022



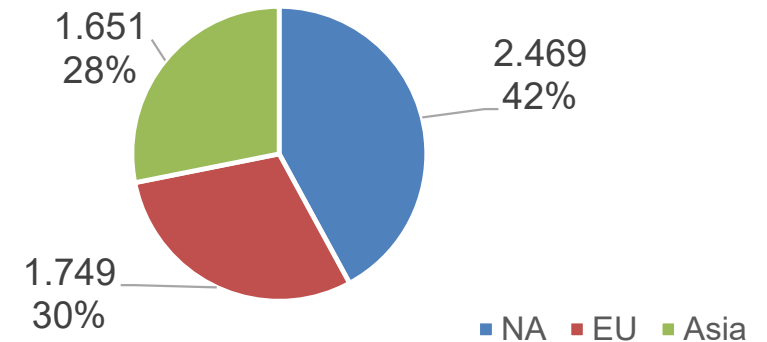
# Pharma Development Pipeline Phase I-III 2023

Total Molecules:  
**4.301**

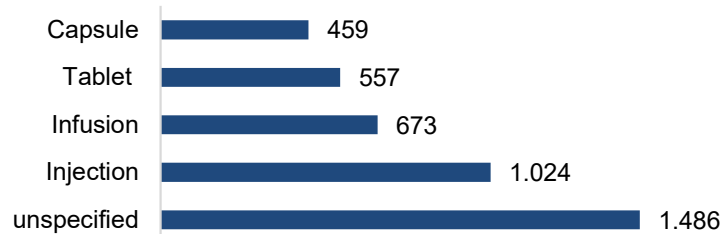
Molecules in development



Country split clinical trials

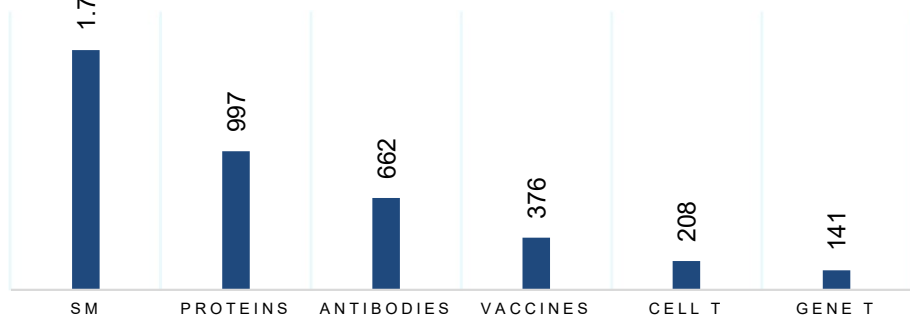


Molecules per formulation

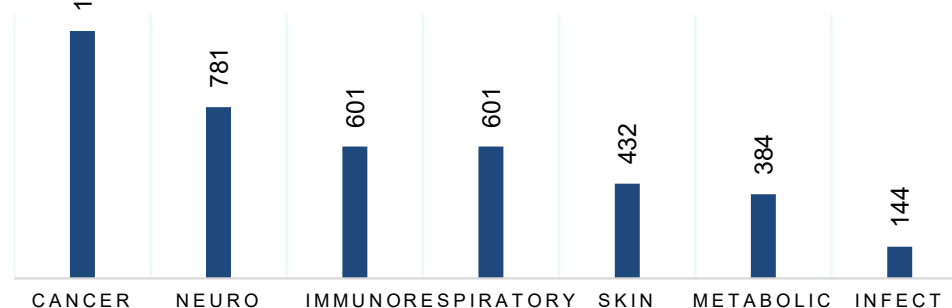


# Pharma Development Pipeline Phase I-III 2023

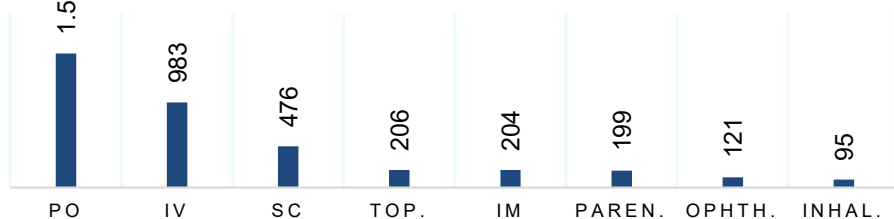
### MOLECULES BY DRUG CLASS




### MOLECULES BY TARGET INDICATION



### MOLECULES PER ROUTE OF ADMINISTRATION



## Bringing a New Drug to Market is Complex and Costly

 Key market trends in the biologic market



### Increasing costs

It can cost  
**\$2.6 billion**  
to bring a new drug to market<sup>1</sup>



### Drug development takes a long time

It takes an average of  
**over 10 years**  
from first patent filing to market<sup>2</sup>



### Drug development is increasingly risky


**Only 10%**  
of drugs entering clinical testing  
receive regulatory approval<sup>3</sup>





### Impact of Delays


**\$1.1 million**  
lost sales for each day a drug's development  
and launch is delayed<sup>1</sup>


## Our Healthcare Industry is Evolving – some trends related to PFS

 **Trend to self-administration / combination products:** 49% of injectables in market can be self-administered, led by PFS, Auto Injector

 **Trend from IV to subcutaneous:** SC MAb approvals > IV since 2017 (8% vs. 6%) driven by Life Cycle Management, biosimilar adoption and hospital to at-home care trend.


 **Large volume delivery for PFS:** driven by home care injection of high viscose drug, a consequence of the above trend for IV to subcutaneous

 **CCI and stability of PFS for extreme cold storage** driven by mRNA vaccines and other new therapies

 **Increased focus on sustainability:** Sustainable packaging, social responsibility efforts, and environmental actions


 **Regulatory complexity is increasing:** new EU GMP Annex 1 and Article 117 Medical device regulation and ISO standards 11608


 **CCI and stability of PFS for extreme cold storage:** driven by mRNA vaccines and other new therapies


 **Advancements in silicone free solutions**





## Our Healthcare Industry is Evolving – some trends related to PFS cont.


 **Advancements in silicone free prefilled syringe solutions** to protect complex and sensitive biologics from silicone-induced protein aggregation and particle formation


 **Innovations in ophthalmic drug delivery:** increase the challenges and drive the innovations in ophthalmic drug delivery

 **Innovation & collaboration:** importance of choosing the right partner to develop new products to solve problems

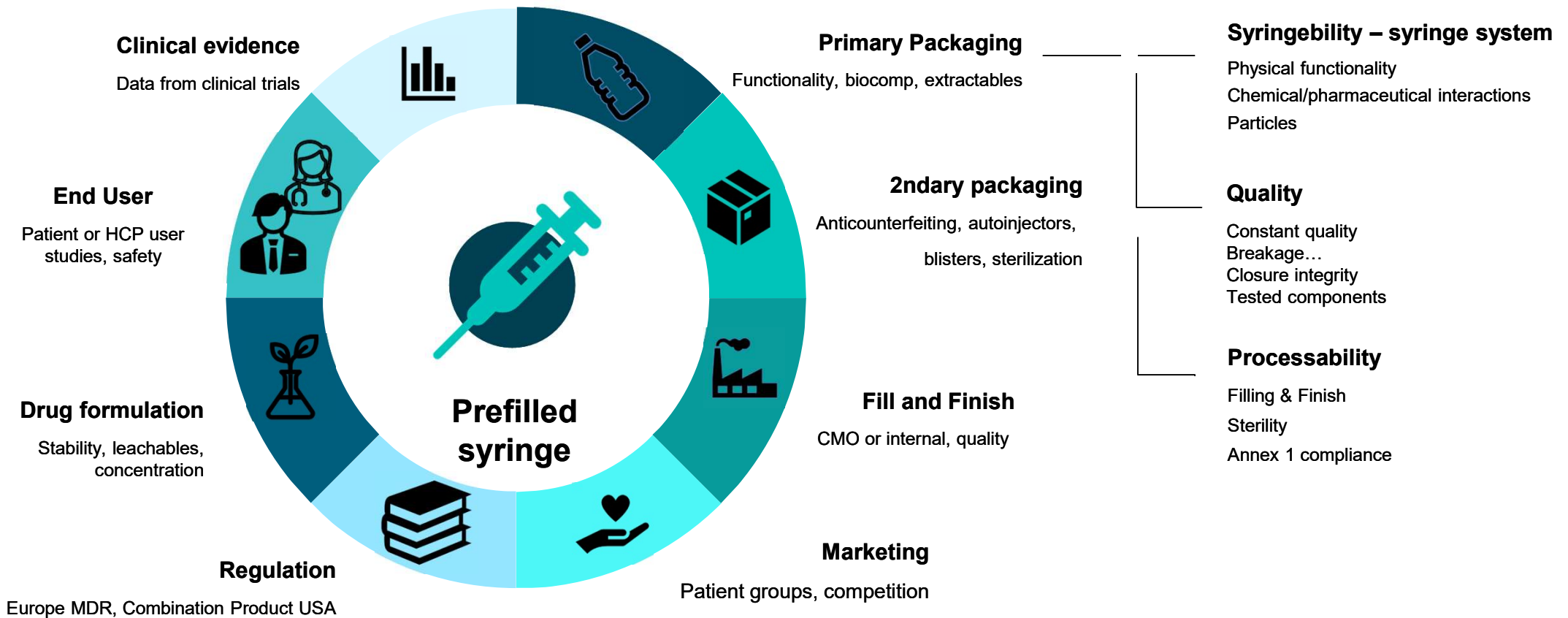
 **Alternatives to EtO sterilization:** raised over the years multiple times, effects like residuals of ETO and ECH and not environmentally friendly

 **Advancements on Radio Frequency Identification (RFID) added to PFS:** enabling unit-level traceability and data analytics for manufacturing and disease management.

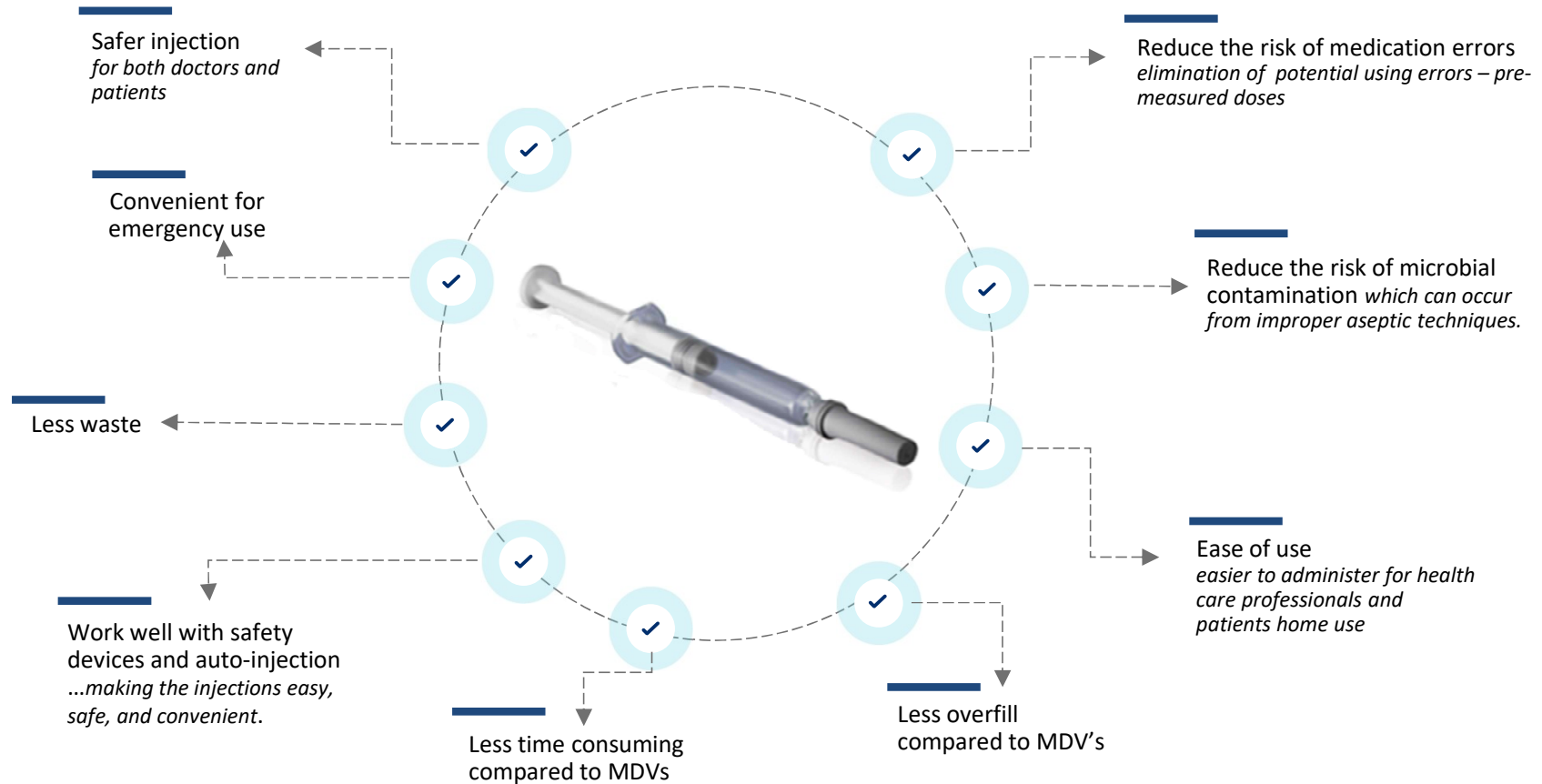
 **Digital health and smart devices:** are playing a pivotal role in the digitalization of health. Utilizing data collected from delivery devices and connected platforms holds significant promise for enhancing patient engagement and placing the end user at the center of focus

 **Advancements in manufacturing** including fully robotic manufacturing and assembly lines

# Interfaces and Stake holders to get to a final drug product in a PFS



# Multi Dose Vials MDV's vs Prefilled Syringes: Some Advantages

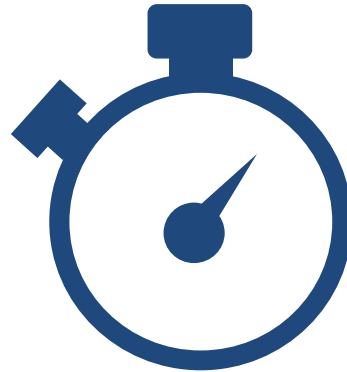


## Convenience / Ease of Use / Patient Satisfaction (e.g. Copaxone®)



Preparing injection for  
COPAXONE® filled in a vial

**235 sec.**



Preparing injection for  
COPAXONE® filled in PFS

**38 sec.**

A typical patient can save about **20h a year** by using  
Copaxone® in a PFS format

## Diverse Syringes for Diverging Needs

Application/requirement	Heparins - anticoagulants	Vaccines – mainly flu vaccines	Biologics – very diverse group	Aesthetics – beauty and lifestyle	Diabetes/ Obesity
Route of administration	Subcutaneous injection, 1/2” needle	Intramuscular injection, 5/8” needle	Mostly subcutaneous injection, 1/2” needle	Subcutaneous injection, diverse needles SC, ID	Subcutaneous injection, 1/2” needle
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 (and higher) (0.5 ml – ophtha)	Luer Lock 1 mL Long	1 mL long with staked-in needle
End user	Health care prof. Patient	Health care prof.	Health care prof. Patient	Health care prof.	Patient
Batch size	High volume	High volume	Small batch sizes	Mid batch size	High volume expected
Device application	Safety device integration	Back Stop Disposable needle	Often auto Injector use	Possible	Autoinjector
Very high focus on	Processability & speed	Processability & speed	Sensitive drugs, often small fill lines	Appearance	Processability
Price sensitiveness	high	medium	low to medium	medium	medium
Remarks	Few players, mass market	Few players, mass market	Specialty ophthalmics (cataract, intravitreal): luer lock, dose mark, particle limits	Hyaluronic acid not oxygen sensitive	Hormones, few players so far; syringes, also Cartridge based devices

# Decision making – does a syringe make sense?

Prefilled glass syringe	Advantage	Filled glass vial, closed	Advantage	Prefilled glass syringe	Advantage	Filled glass vial, closed	Advantage
<b>Total cost for container</b>				<b>Contact materials</b>			
Low overfilling, low residual volume	+	High overfilling, high residual volume	-	Contact with the drug during storage:	-	Contact with the drug during storage:	+
Higher costs for packaging materials	-	Lower costs for packaging materials	+	Glass		Glass	
				Elastomer stopper		Elastomer stopper	
				Elastomer cap			
				Tungsten (extractables)			
<b>User-friendliness</b>				<b>Special applications</b>			
Single dose	+	Single or multiple dose	+ -	Silicone oil (glide agent)		Highly viscosity drugs	-
Few steps through to injection	+	Many steps in injection preparation	-	Needle adhesive,		Lyophilization, reconstitution simple	+
Low risk of incorrect dosing	+	Higher risk of error for correct dosing	-	Stainless steel		Training necessary, especially for the uninitiated	-
No other components needed (needle syringe) at point-of-care, exception: push-on cannula for Luer syringes	+	Disposable components necessary at the point of care:	-				
		Plastic single-use syringe		Highly viscosity drugs, low volume	+		
		Cannula for filling		Lyophilization, reconstitution complex	-		
		Injection cannula		Autoinjector, simplicity, home use	+		
				<b>Overall advantage</b>	<b>7   3</b>	<b>Overall advantage</b>	<b>3   6</b>

# Decision making – Glass or COP?

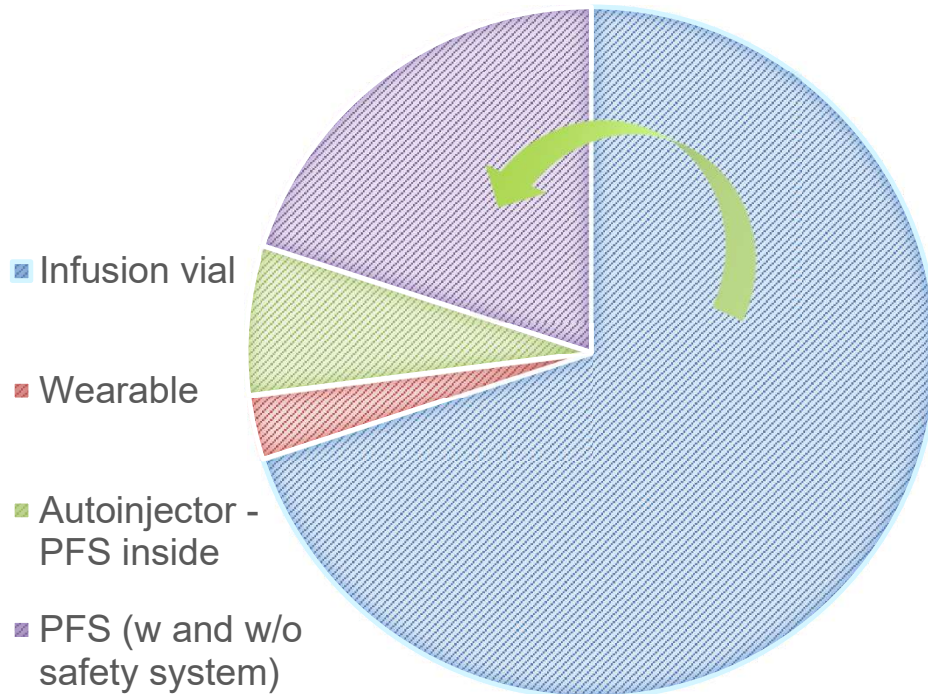
	Advantage of glass	Advantage of COP	Remarks
Risk of breakage during filling	+ --	+ --	Line clearance after glass breakage during filling is expensive but rare
Risk of breakage at the point of care	+ --	+ --	Possible, but rare with small volume syringes. Breaking force minimized in advance during development
Luerlock integrated	-	+	Slipping of the thread and detachment impossible with COP
Tungsten	-	+	Alternative pin materials available today, no tungsten in COP injection molding
Adhesive	-	+	COP syringe free of adhesive
Silicone oil	+ --	+ --	COP syringes silicone oil free, long available
Gas and especially oxygen barrier	+	-	Glass unsurpassed
Extractables	+	-	Low for glass and known, inorganic
pH shift	-	+	No pH shift with COP
Experience	+	-	Experience with glass in the pharmaceutical industry is extensive, also for filling lines

	Advantage of glass	Advantage of COP	Remarks
Costs	+	-	COP more expensive than glass
Design freedom	-	+	Injection molding allows diverse designs
Tool	+	-	Free molding needs no special, expensive injection molding tools
Tolerances	-	+	Glass with wider tolerances through free molding
Scratch resistance	+	-	Plastic sensitive, however scratches do not affect the breaking force
Sterilization of the packaging material	+ --	+ --	Glass: EtO** COP: gamma, steam
Terminal sterilization	+ --	+ --	Glass: steam, EtO, other methods COP: steam, gamma, other methods
<b>Overall advantage</b>	<b>6   6</b>	<b>6   6</b>	

OP = Cyclic Olefin Polymer  
\*\*EtO = Ethylene Oxide

# Decision making – does a syringe make sense?

Basic market share, vial presentations are transferred into syringes during life cycle management:



## 1. Safety first

## 2. Where is the point of care -who is the end-user?

Hospital -hcp- health care professional? *Vial ok*  
 Home use -patient? *Syringe (sc) better*

## 3. What is most economic? Vial or syringe better?

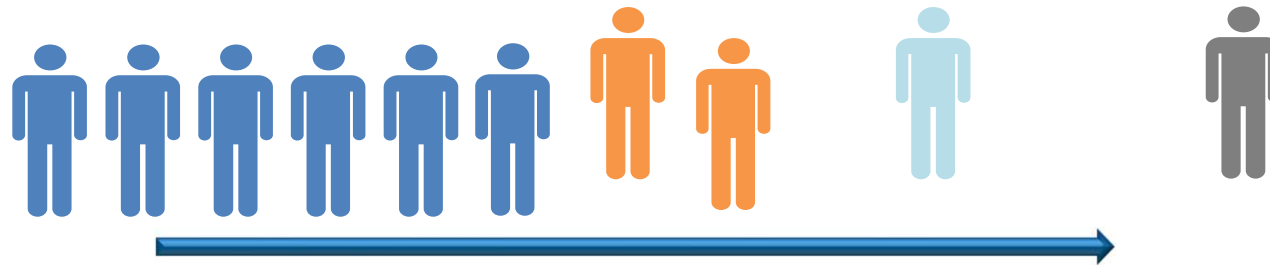
Who pays? Health system or self payment?  
 Cost pressure towards self use

## 4. Drug formulation possible in syringe?

Life cycle management from vial to syringe



# Holistic view on advantages of Prefilled syringes



	Infusion – vial (or bottle, bag)	Prefilled Syringe	Safety syringe (PFS)	Auto-injector – syringe inside	Wearable – vial or cartridge inside
<b>Main use</b>	Hospital	Home use, doctor, hospital	Hospital, home use	Home use	Home use
<b>Home use</b>	rare	yes	yes	convenient	convenient
<b>Injection time</b>	Infusion 	10 s (sc) 	10 s (sc) 	10 s (sc) 	minutes 
<b>Cost of device</b>	\$	\$\$	\$\$\$	\$\$\$\$	\$\$\$\$\$
<b>Cost for health system</b>	\$\$\$\$\$	\$	\$\$	\$\$\$	\$\$\$\$
<b>e.g.</b>	Cancer treatment	Vaccine, Ophthalmic	Anticoagulants - Heparin	Chronic/autoimmune disease	Autoimmune disease/specialties

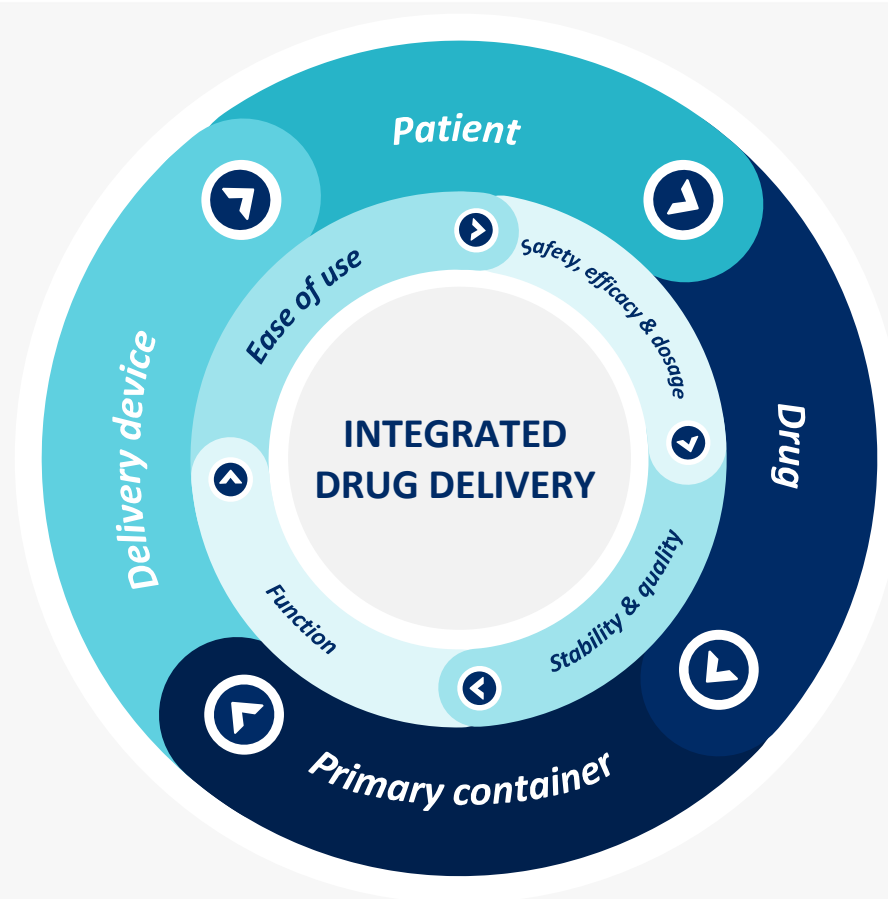
## Primary Containment & Patient Experience



Container closure systems are the heart of drug quality and combination products. They offer:

- Stability
- Protection
- Integration with delivery device
- Safety
- Quality

**Critical to the Patient Experience**



# Summary

- Growing double digit market for PFS
- Polymer syringes market is increasing but don't mix with disposable syringes
- Biological drive pharmaceutical value growth and biologics need PFS (in e.g. autoinjectors)
- Our Healthcare Industry is Evolving – a lot of trends related to PFS
- GLP 1 agonists as rather new big market
- Many parameters to check if a PFS makes sense
- Advantages of PFS over vials

# Sources

- West internal
- Gerresheimer internal
- Source: IQVIA 2022 Global Audited Sales
- ISPE Discussion Paper: Unique ID on Primary Containers to Drive Product Traceability and Quality – Feb 2021 – Stevanato Groupe
- Based on data from Tufts Center for the Study of Drug Development
- Emerging Biopharma’s Contribution to Innovation, June 2022, IQVIA.
- Biotechnology Innovation Organization: Clinical Development Success Rates
- Zeiß, Bernd: Silikonölfreie vorgefüllte Spritzensysteme Pharm. Ind. 84, Nr. 8, 1021–1029 (2022).ECV • Editio Cantor Verlag, Aulendorf (Germany)