

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



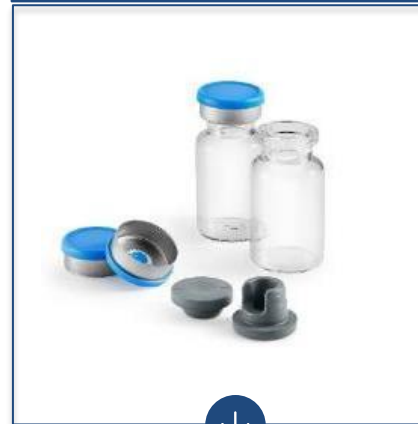
Cartridges



- › Elastomeric Components:
- › Plungers Lined Seals



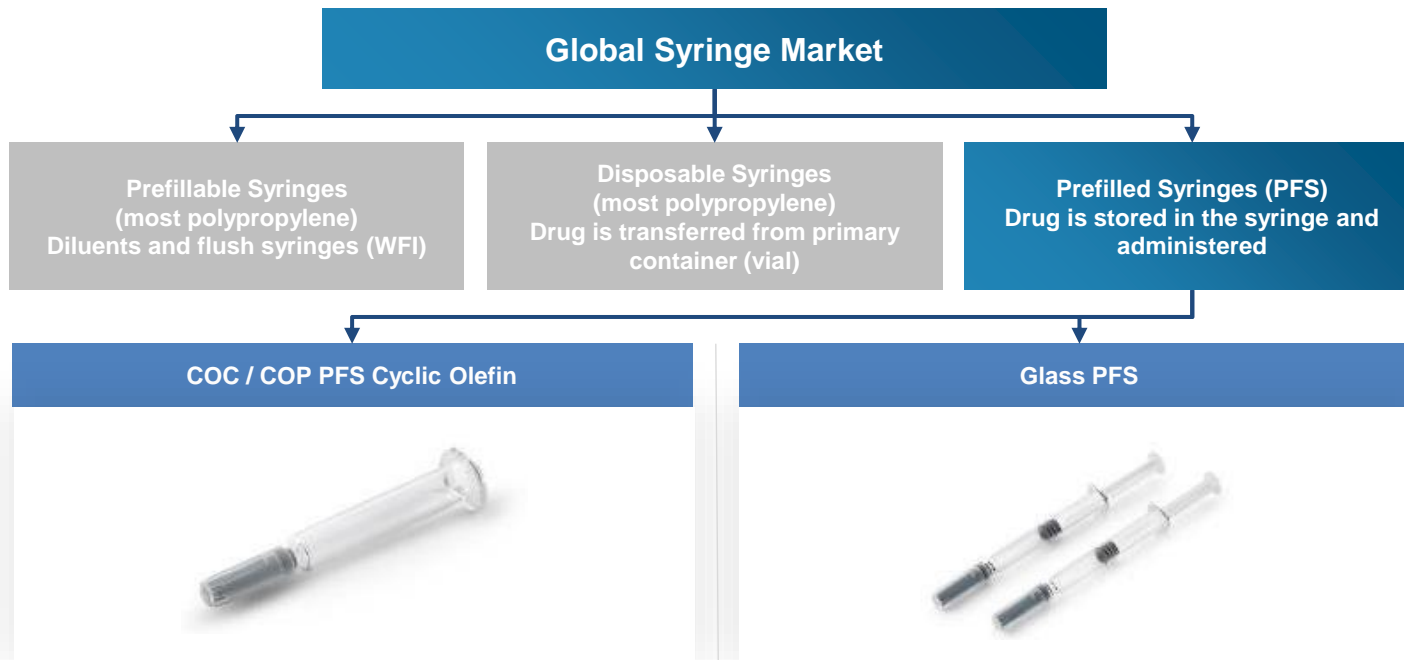
Vials



- › Elastomeric Components:
- › Lyophilization or Serum Stoppers



Syringe Market Overview



COC = Cyclic Olefin Copolymer COP = Cyclic Olefin Polymer

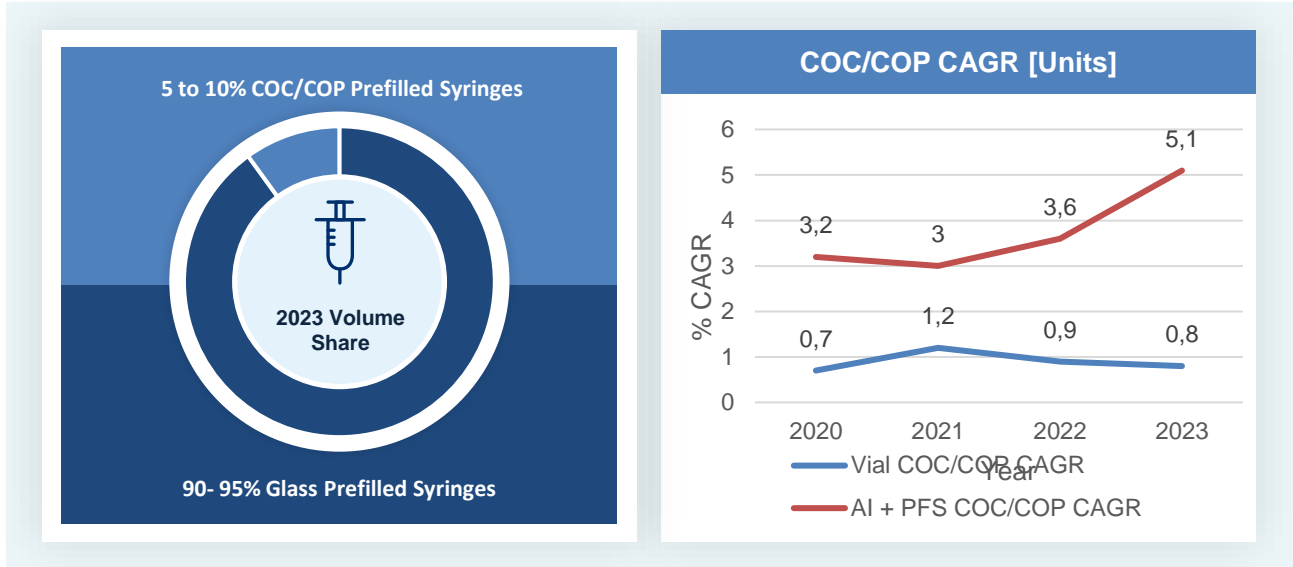
PFS Polymer vs. Glass – Market Estimates



The market share of polymer containers (PFS, vials, cartridges) is increasing

The global PFS volume is estimated to be ~ 5Bn units currently.

The global PFS market was valued at US\$ 13.6 Bn in 2021 and is anticipated to reach more than US\$ 35.7 Bn by end of 2031 [CAGR 10.1%].*



Based on market experience, internal knowledge and IQVIA data

*Prefilled Syringes Market | Global Analysis Report 2031 (transparencymarketresearch.com)

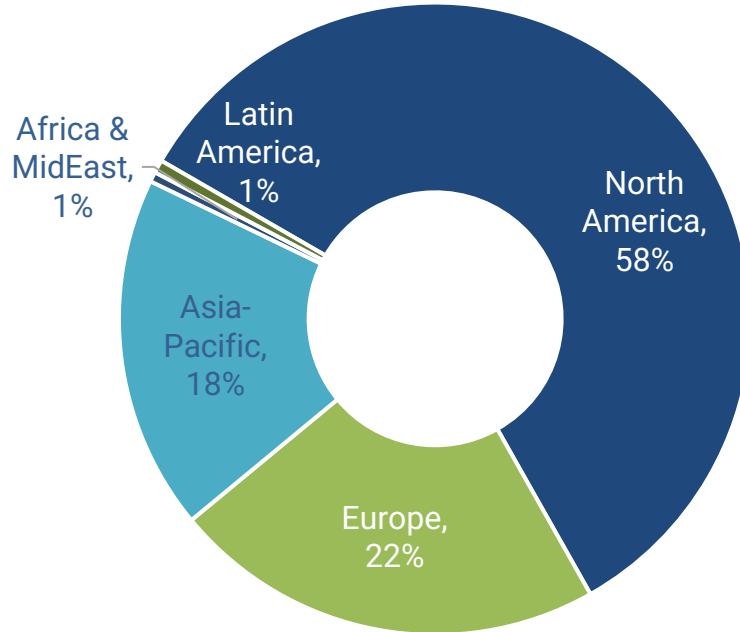
Glass Dominates Most Therapy Areas, but COC/COP preferred in Advanced Therapies

COC/COP	Market Section	Glass
+	Small Molecules	+
+	Traditional Biologics (Cancer, Auto-immune)	+
+	Pharma Cosmetic Segment (Dermal Fillers, Hyaluron, Liquid Botox)	+
+	Advanced Therapies [e.g., cell and gene therapies, RNA]	+



Most of the market is in glass and will continue so, but COC/COP is the preferred containment solution for sensitive molecules, highest quality specifications and where challenging storage conditions e.g., cold temperature, are required

Injectable Value Share By Region, 2022

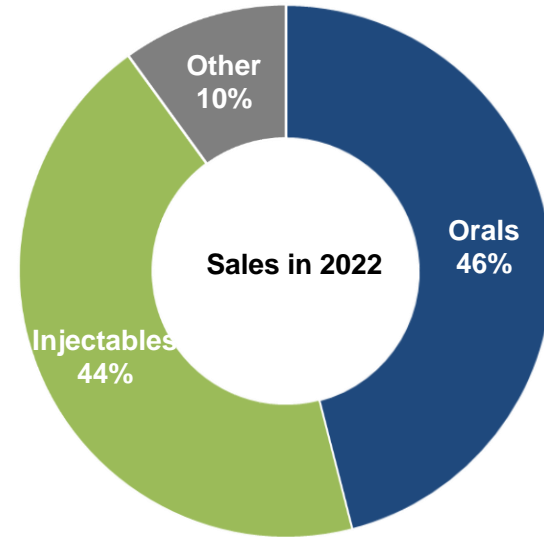
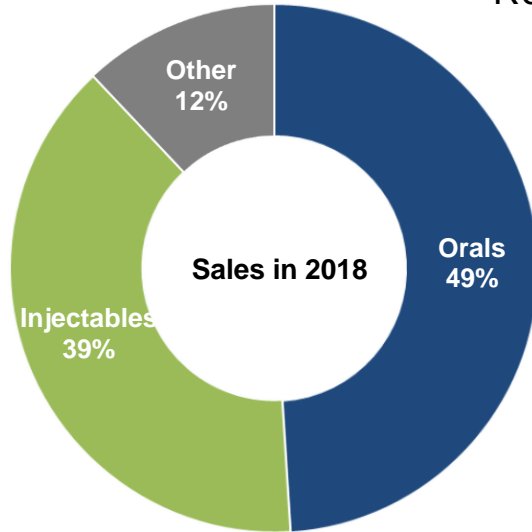


As of 2022, North America is the largest market by value, while Asia is the largest market by volume

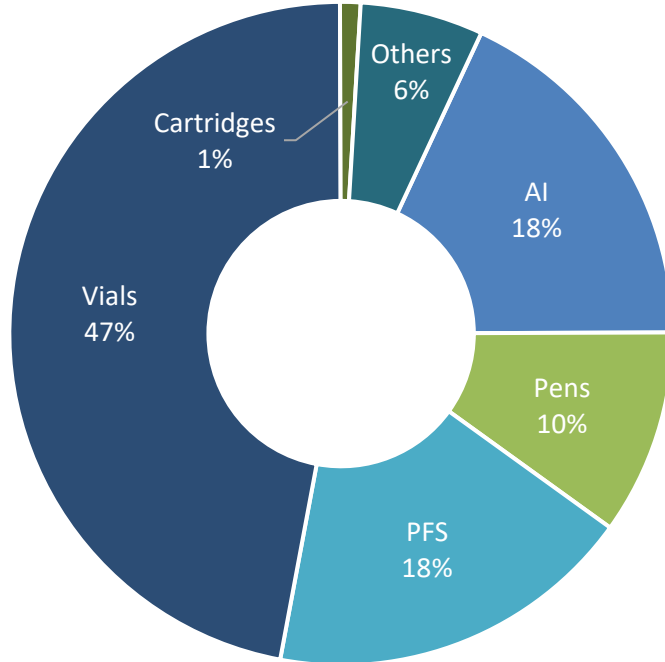
Regions	2018 - 22 CAGR
Global	9%
North America	11%
Europe	7%
Asia-Pacific	4%
Africa & MidEast	8%
Latin America	11%

Share of Injectables is expected to increase through 2022

Global Market Share% by
Route of Administration



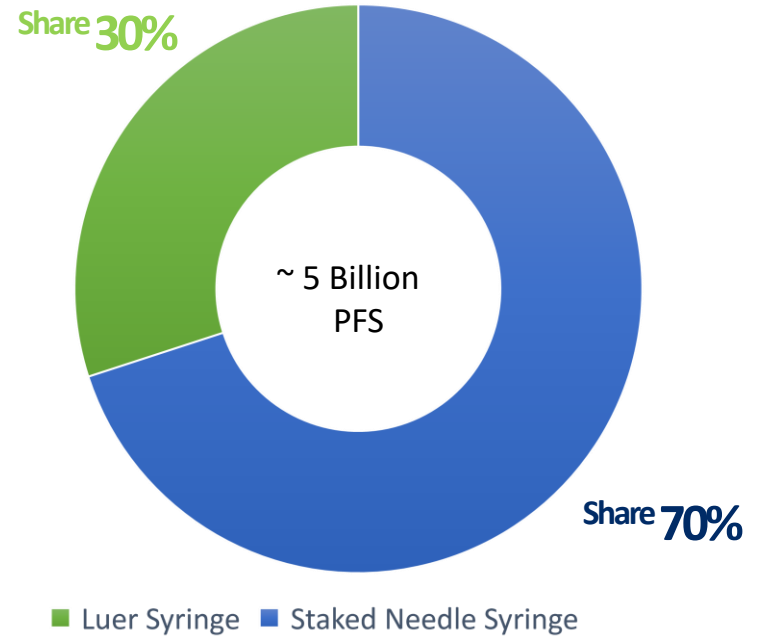
Global Injectable Value Share By Format, 2022



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

Global Prefilled Syringe Luer vs Staked Needle

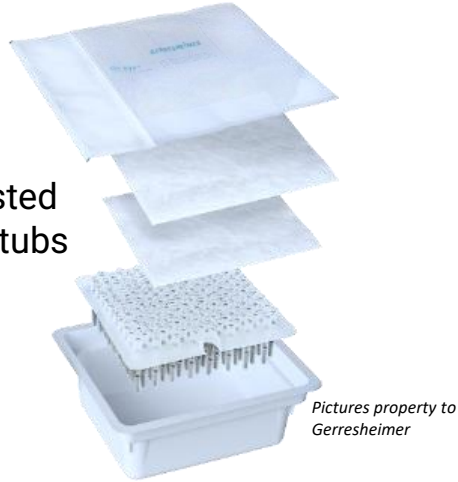
- > The global prefilled syringe market is estimated to continuously grow at mid-single digit
- > Most staked needle syringe applications use RNS



Data Source: West best estimate, multiple sources

Global Prefilled Syringe Luer vs Staked Needle

- > Ready-to-Use Nested glass syringes in tubs

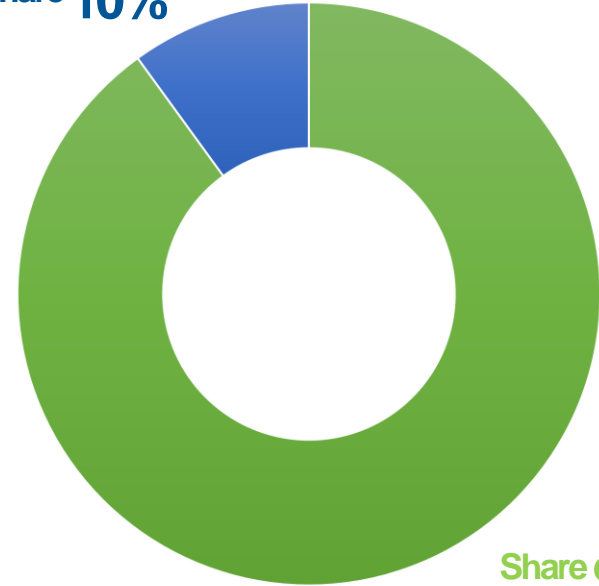


Pictures property to Gerresheimer

- > Bulk glass syringes on rondo trays



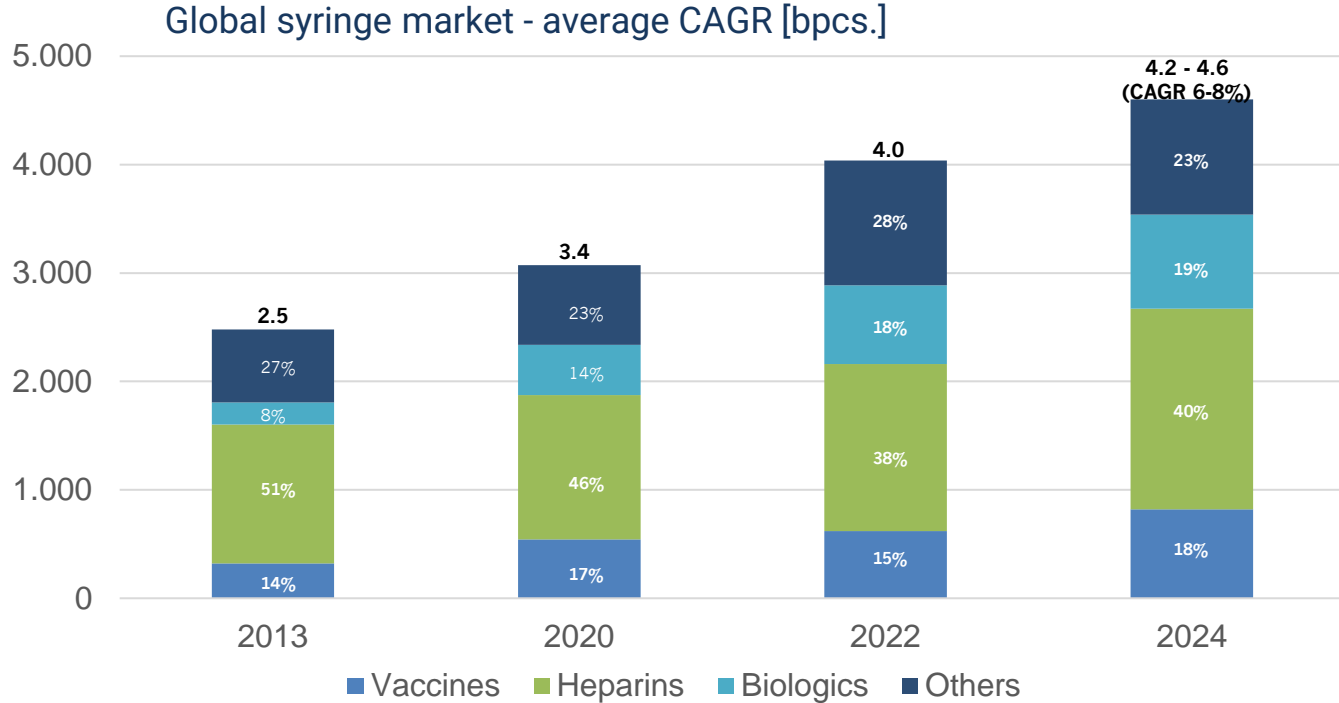
Share 10%



Share 90%

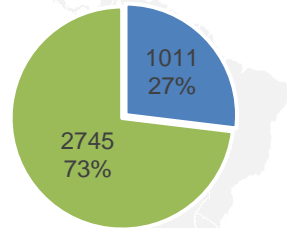
■ nested syringes ■ bulk syringes

Syringe market demand per indication



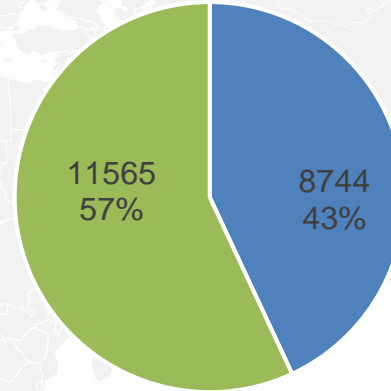
Biologic / Non-Biologic market total in 2022

AMOUNT OF MARKETED DRUGS IN 2022



■ Biologics ■ Non-Biologics

AMOUNT OF DRUGS IN DEVELOPMENT 2022

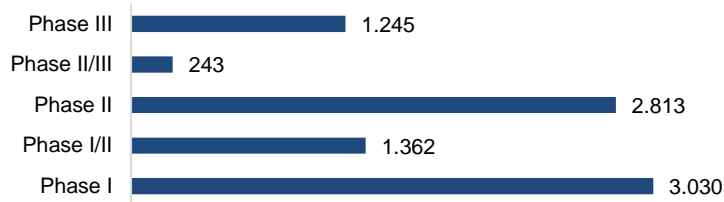


■ Biologics ■ Non-Biologics

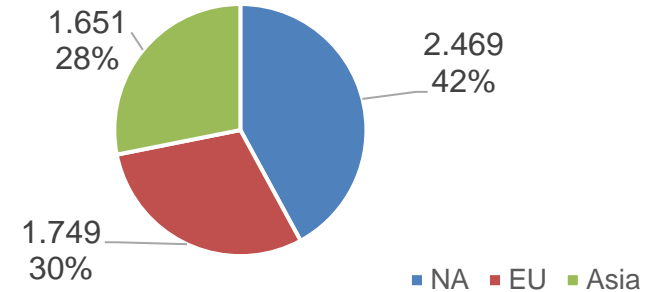
Pharma Development Pipeline Phase I-III 2023

Total Molecules:
4.301

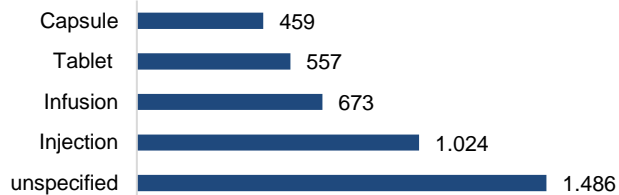
Molecules in development



Country split clinical trials

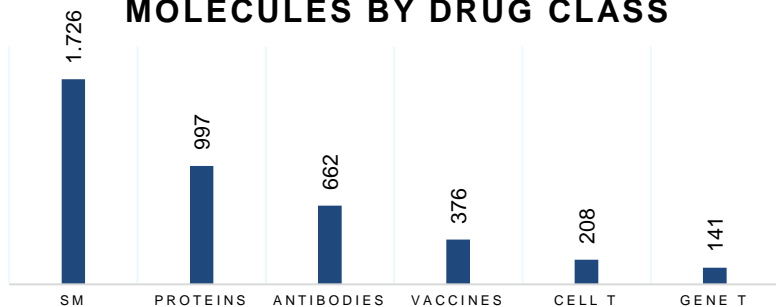


Molecules per formulation

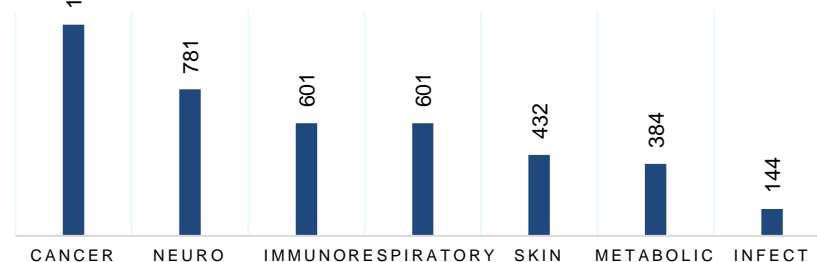


Pharma Development Pipeline Phase I-III 2023

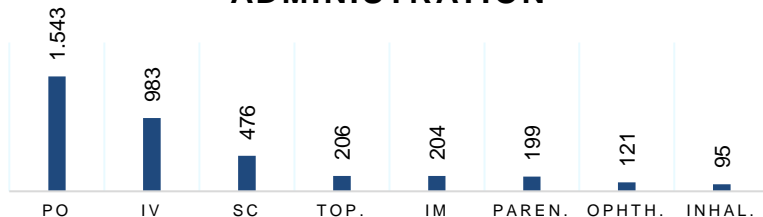
MOLECULES BY DRUG CLASS



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 market¹



Drug development takes a long time

It takes an average of
over 10 years
from first patent filing to market²



Drug development is increasingly risky

Only 10%
of drugs entering clinical testing
receive regulatory approval³



Impact of Delays

\$1.1 million
lost sales for each day a drug's development
and launch is delayed¹

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



GLP 1 obesity/diabetes: market explosion syringes and cartridges chosen as primary containers.



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


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

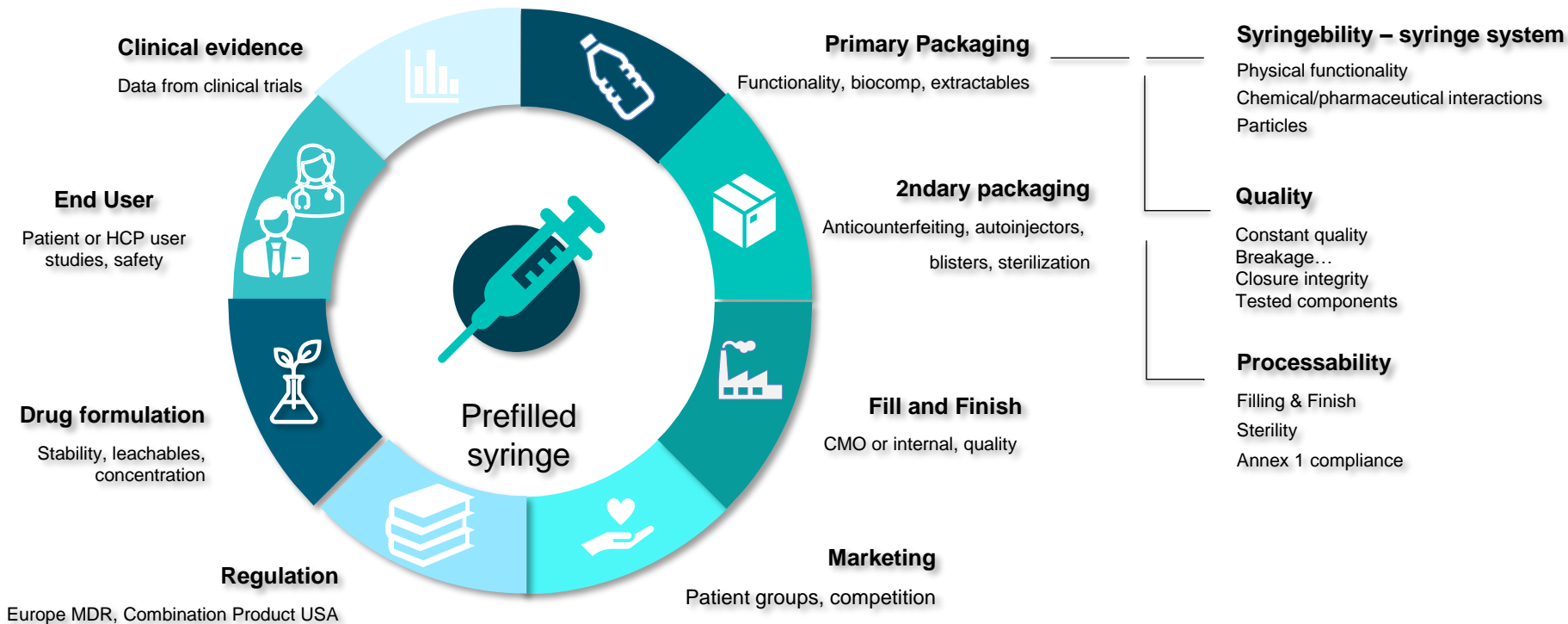
 **Alternatives to EtO sterilization:** raised over the years multiple times, effects like residuals of ETO and ECH and not environmentally friendly

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

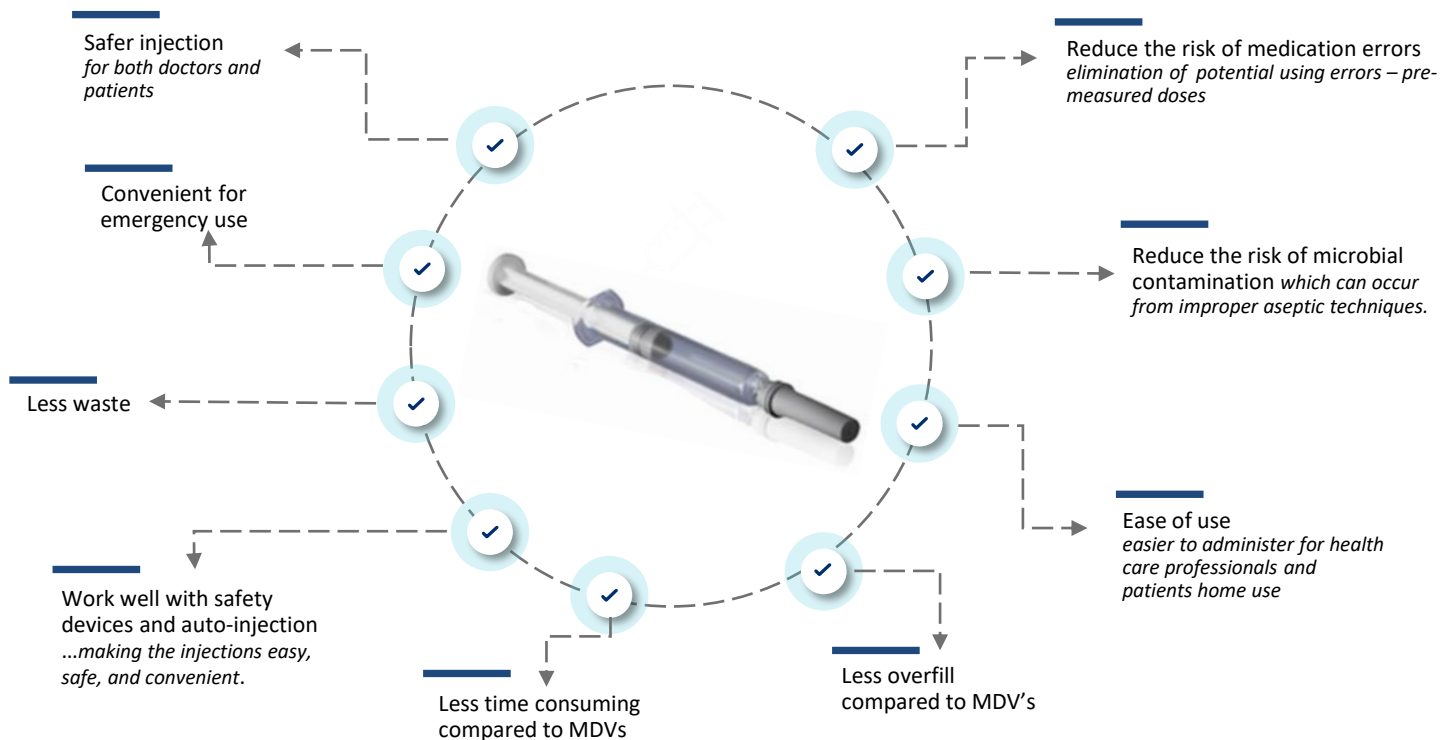
 **Digital health and smart devices** are playing a pivotal role in the digitalization of health. Utilizing data collected from delivery devices and connected platforms holds significant promise for enhancing patient engagement and placing the end user at the center of focus

 **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

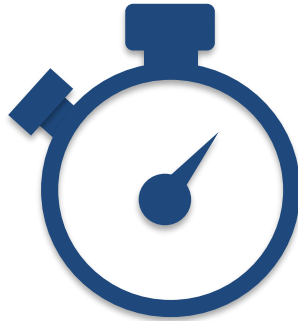


Convenience / Ease of Use / Patient Satisfaction (e.g. Copaxone®)



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 ophthalmic (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
Total cost for container				Contact materials			
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)			
User-friendliness				Special applications			
Single dose	+	Single or multiple dose	+ -	Highly viscosity drugs, low volume	+	Highly viscosity drugs	-
Few steps through to injection	+	Many steps in injection preparation	-	Lyophilization, reconstitution complex	-	Lyophilization, reconstitution simple	+
Low risk of incorrect dosing	+	Higher risk of error for correct dosing	-	Autoinjector, simplicity, home use	+	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					
		Cannula for filling					
		Injection cannula					
				Overall advantage	7 3	Overall advantage	3 6

Decision making – Glass or COP?

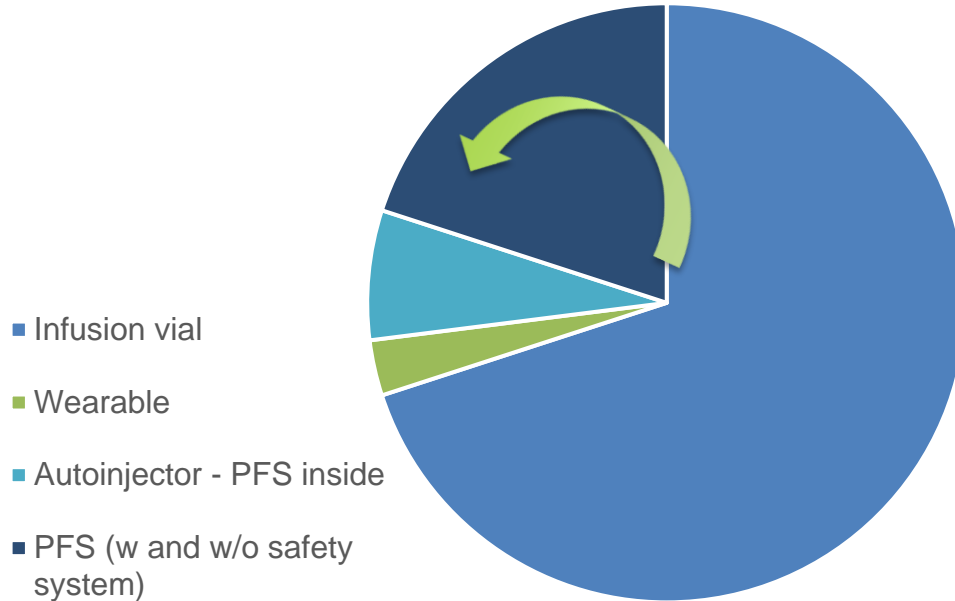
	Advantage of glass	Advantage of COP	Remarks
Risk of breakage during filling	+ --	+ --	Line clearance after glass breakage during filling is expensive but rare
Risk of breakage at the point of care	+ --	+ --	Possible, but rare with small volume syringes. Breaking force minimized in advance during development
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
Overall advantage	6 6	6 6	

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
Main use	Hospital	Home use, doctor, hospital	Hospital, home use	Home use	Home use
Home use	rare	yes	yes	convenient	convenient
Injection time	Infusion 	10 s (sc) 	10 s (sc) 	10 s (sc) 	minutes
Cost of device	\$	\$\$	\$\$\$	\$\$\$\$	\$\$\$\$\$
Cost for health system	\$\$\$\$\$	\$	\$\$	\$\$\$	\$\$\$\$
e.g.	Cancer treatment	Vaccine, Ophthalmic	Anticoagulants - Heparin	Chronic/autoimmune disease	Autoimmune disease/specialties

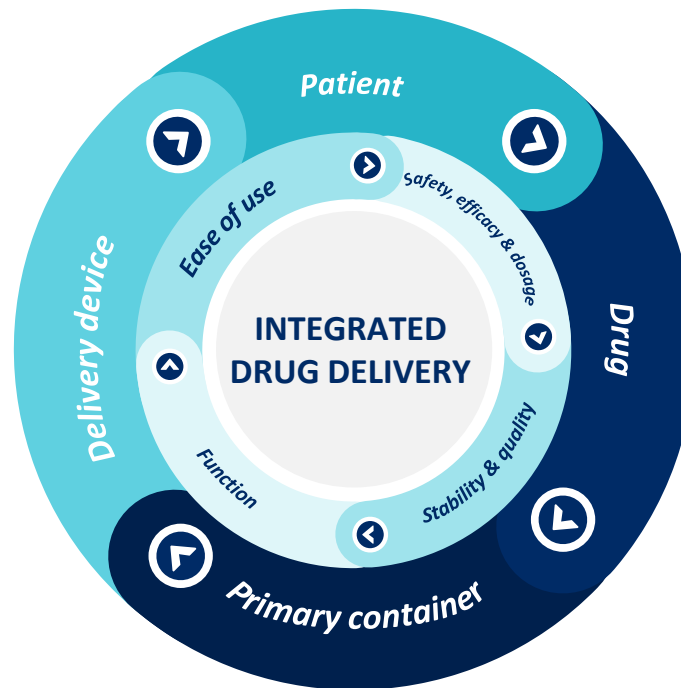
Primary Containment & Patient Experience



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
- 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)