

All about Pre-filled Syringe Systems

From Initial Development to Final Fill Finish

Christa Jansen-Otten

Bernd Zeiss

Basel, May 31st and June 1st 2022



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



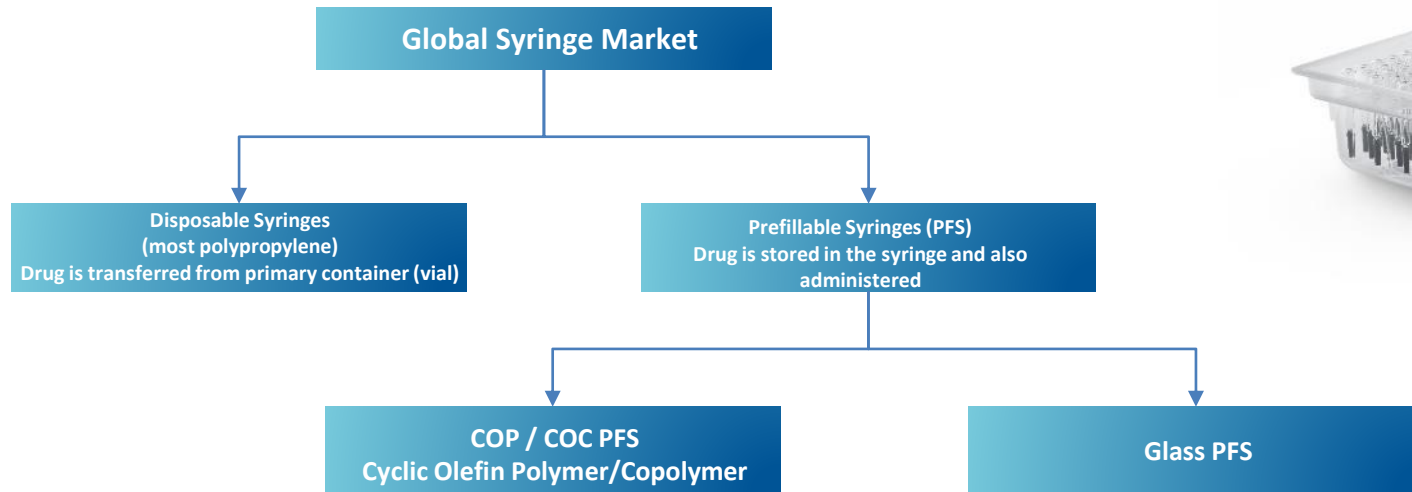
- › Elastomeric Components:
- › Plungers. Lined Seals

Vials



- › Elastomeric Components:
- › Lyophilization or Serum Stoppers

Syringe Market Overview



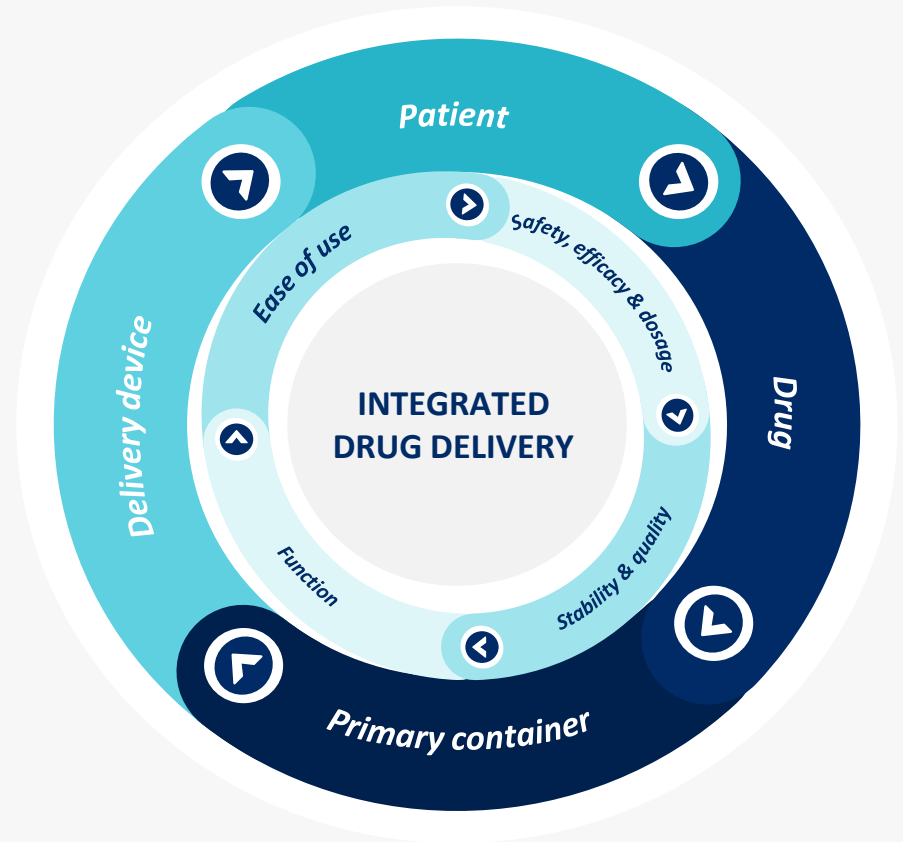
Primary Containment & Patient Experience



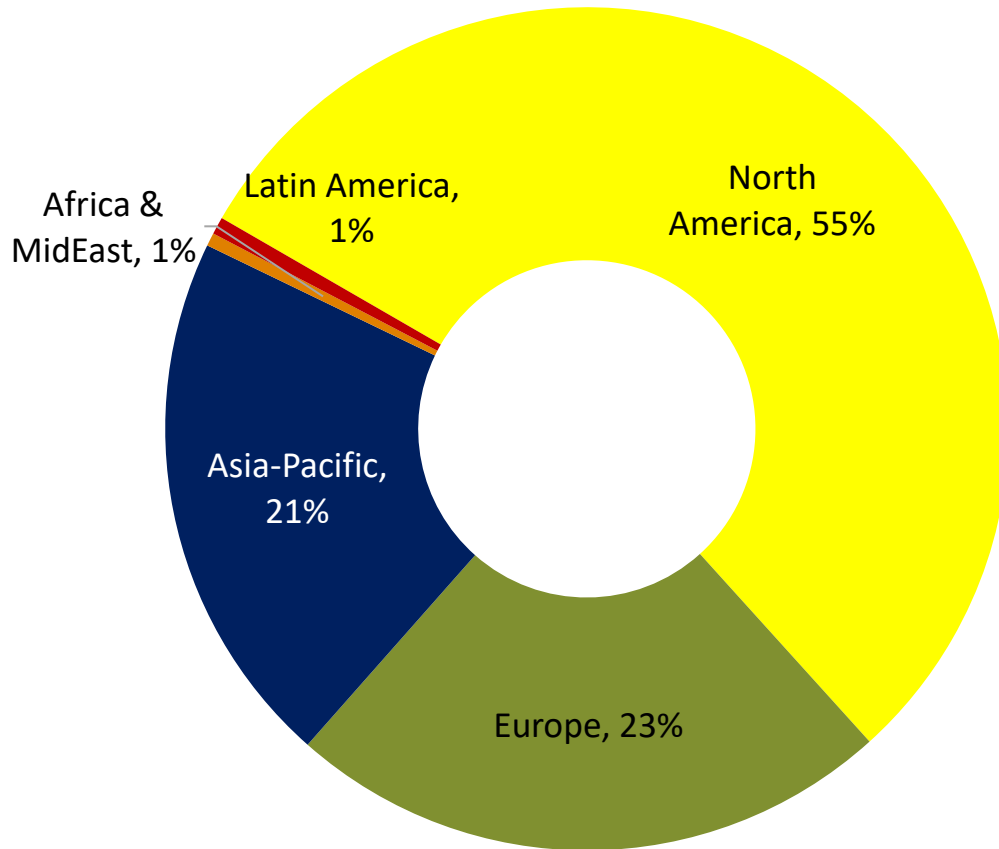
Container closure systems are the heart of drug quality and combination products. They offer:

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

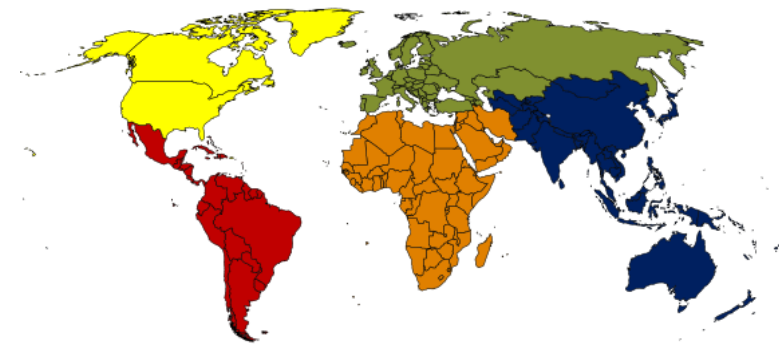
Critical to the Patient Experience



Injectable Value Share By Region, 2021



Regions	2017 - 21 CAGR
Global	10%
North America	11%
Europe	10%
Asia-Pacific	7%
Africa & MidEast	10.5%
Latin America	-4%

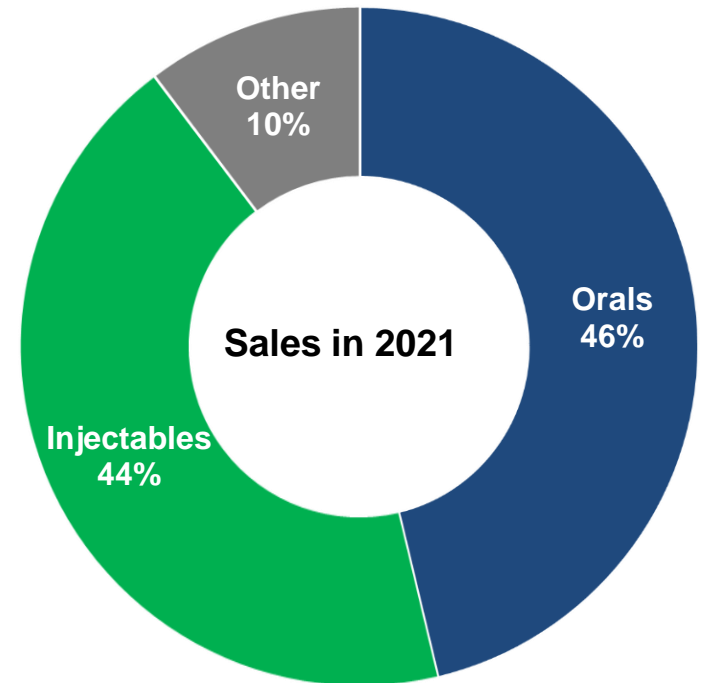
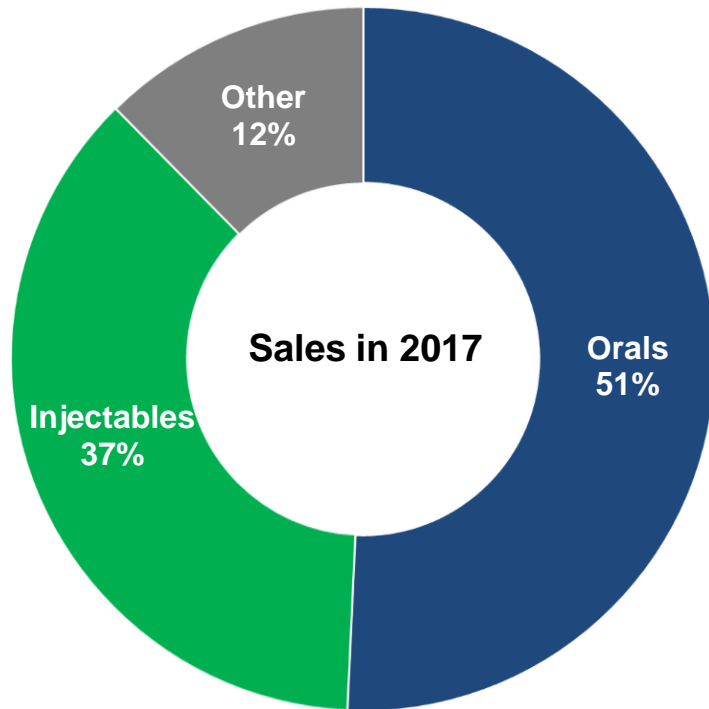


As of 2021, North America is the largest market by value, while Asia is the largest market by volume

Source: IQVIA 2021 Global Audited Sales

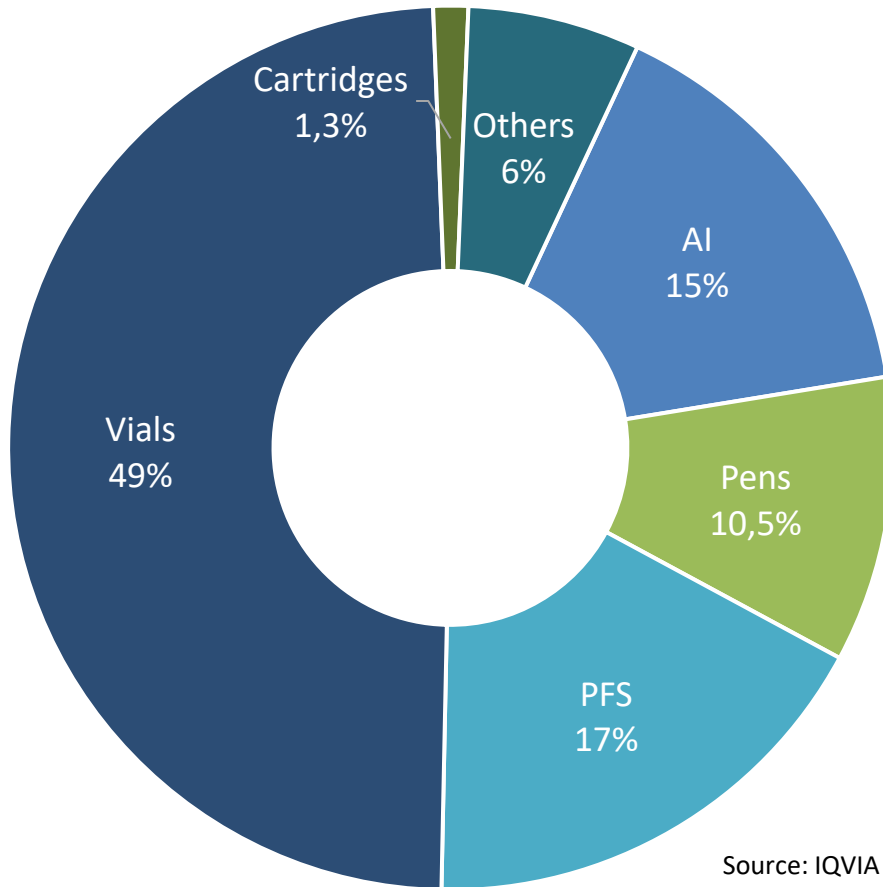
Share of Injectables is expected to increase through 2021

Global Market Share% by Route of Administration



Source: IQVIA 2021 Global Audited Sales

Global Injectable Value Share By Format, 2021

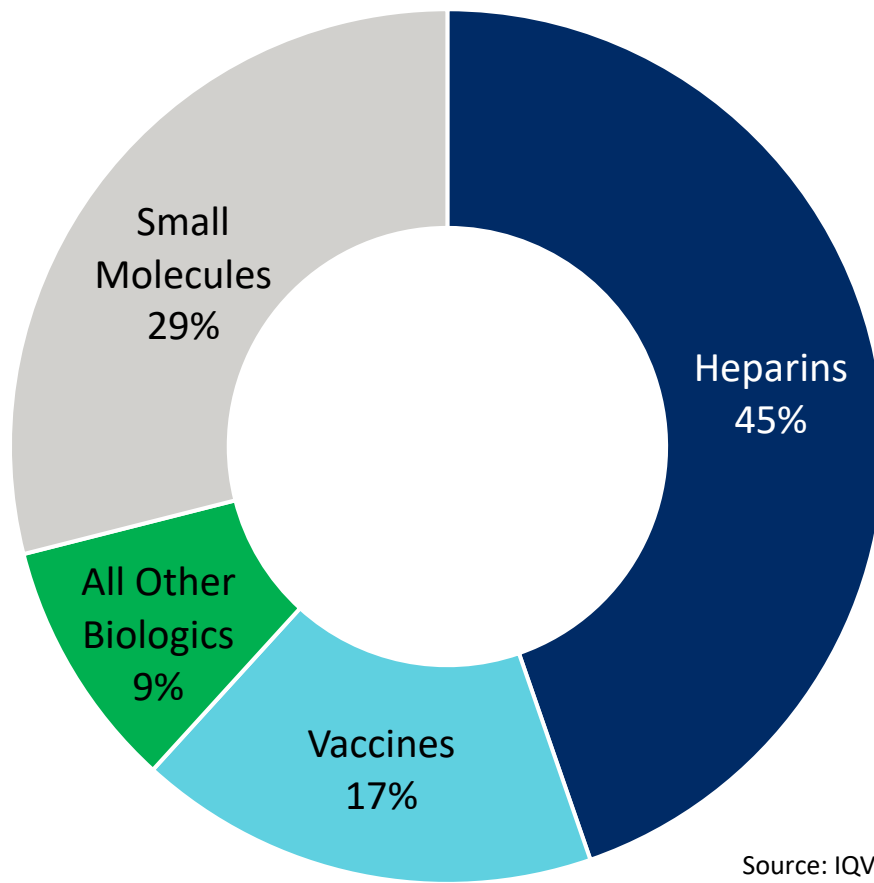


Formats	2017 - 21 CAGR
AI	20%
Pens	13%
PFS	9%
Vials	8%
Cartridges	5%
Other injectables	3%
Grand Total	10%

Source: IQVIA 2021 Global Audited Sales

2020 Global Prefilled Syringe Market Overview

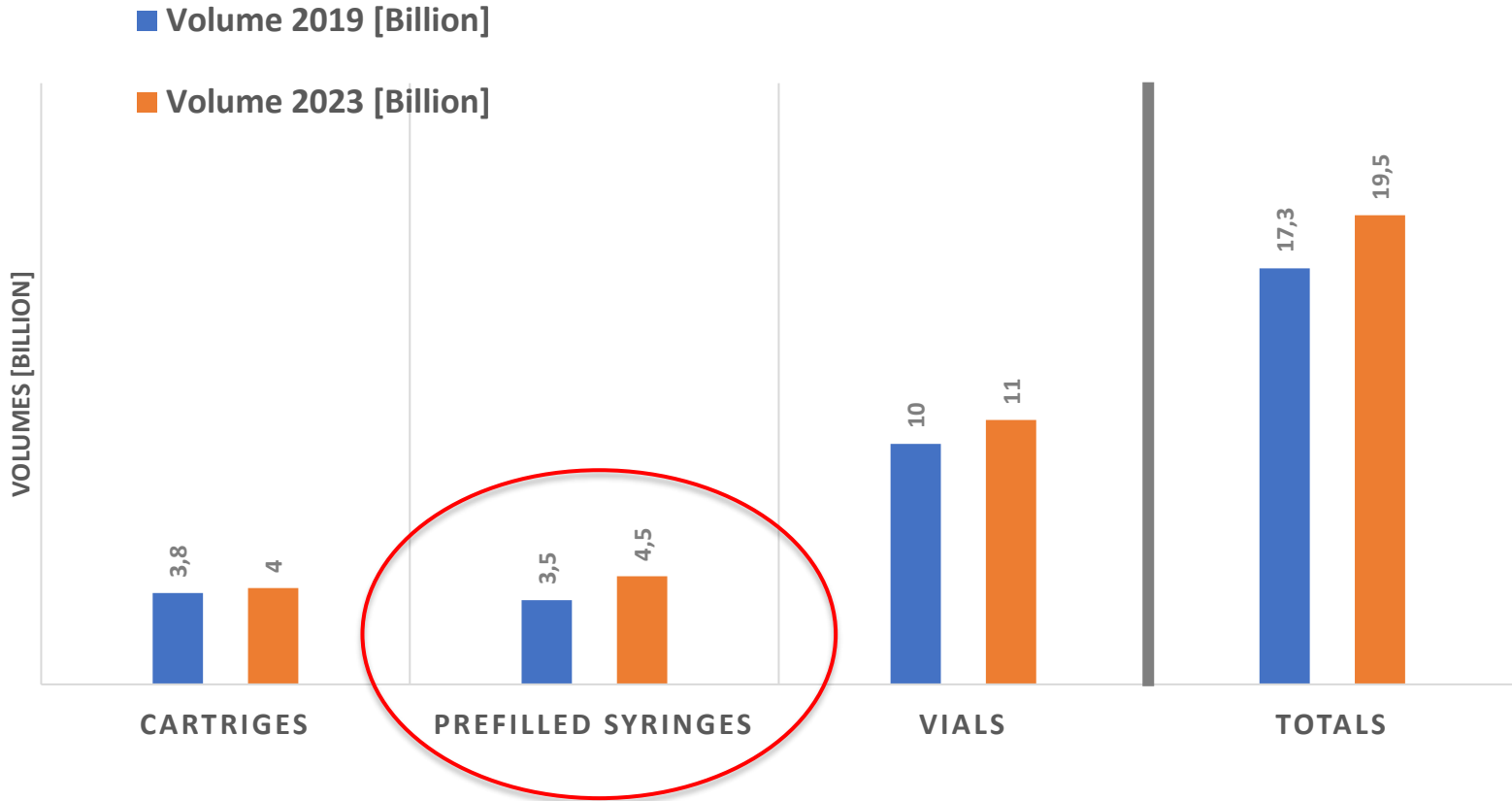
–Market Drivers



Therapy Area	CAGR (2016-2020)
Small Molecules	12%
Heparins	2%
Vaccines	11%
All other Biologics	3%

Source: IQVIA 2021 Global Audited Sales

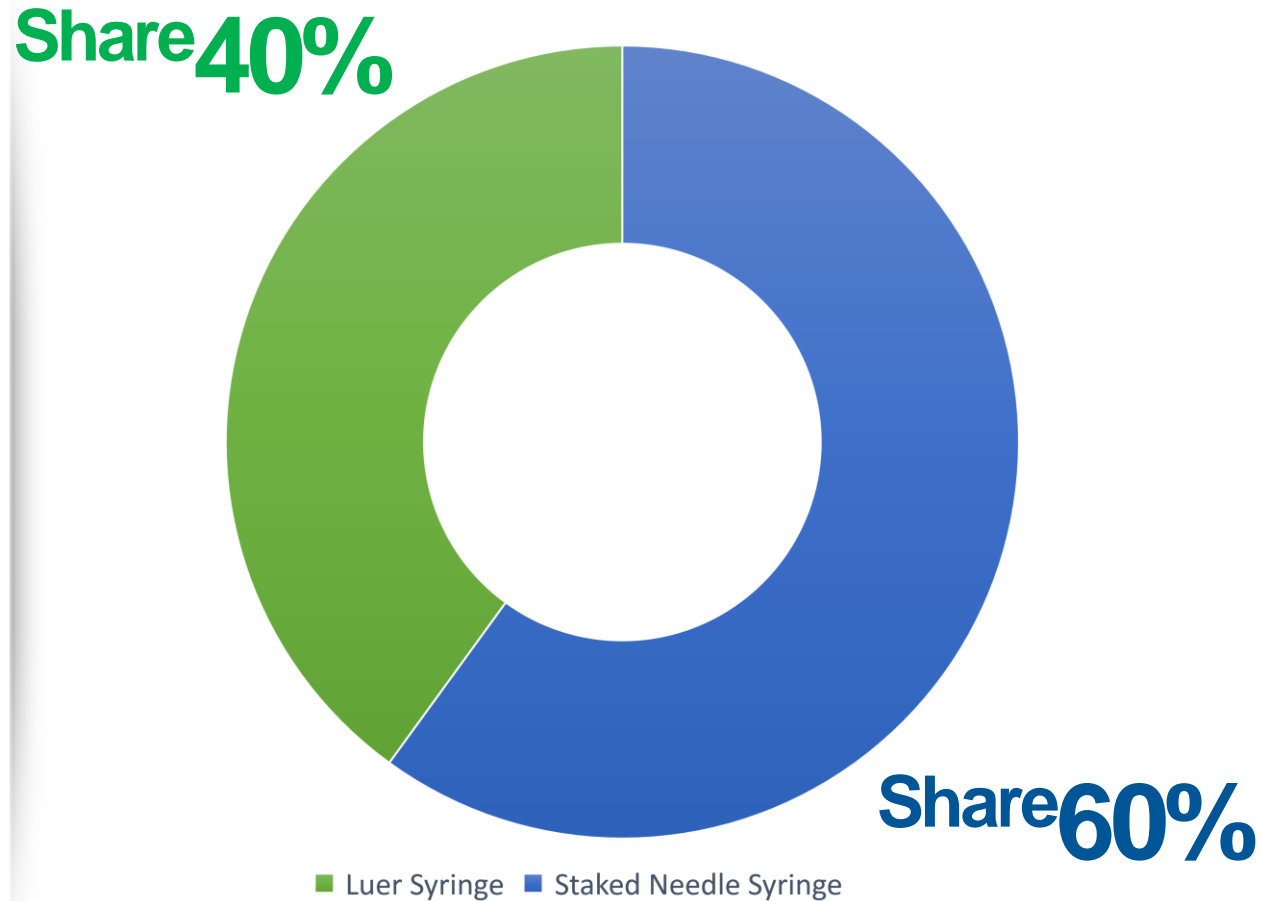
Global Market for Parenteral Containers using Tubular Glass



Source: ISPE Discussion Paper: Unique ID on Primary Containers to Drive Product Traceability and Quality – Feb 2021 – Stevanato Groupe

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: West best estimate, multiple sources

Global Prefilled Syringe Bulk vs Ready-to-Use

Ready-to-Use
Nested glass
syringes in tubs

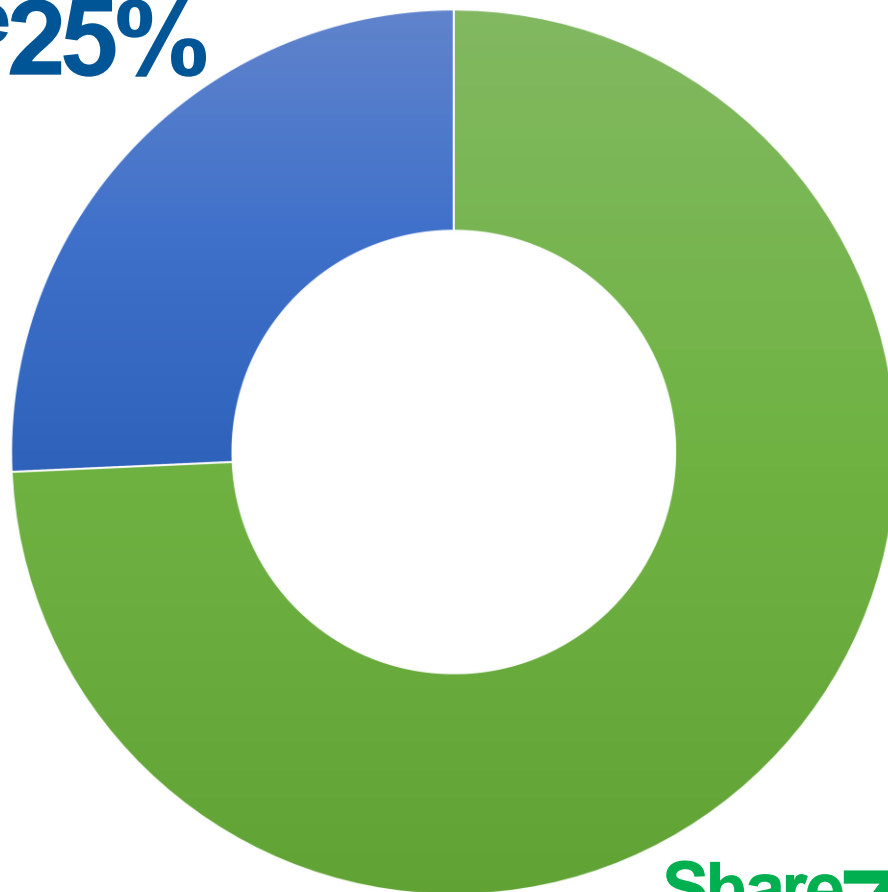


Pictures property to Gerresheimer



Bulk glass syringes on rondo trays

Share **25%**



■ nested syringes ■ bulk syringes

Share **75%**

Bringing a New Drug to Market is Complex and Costly



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 ten years from discovery to market²



Drug development is increasingly risky

- › Only 10% of drugs entering clinical testing receive regulatory approval³



Impact of Delays

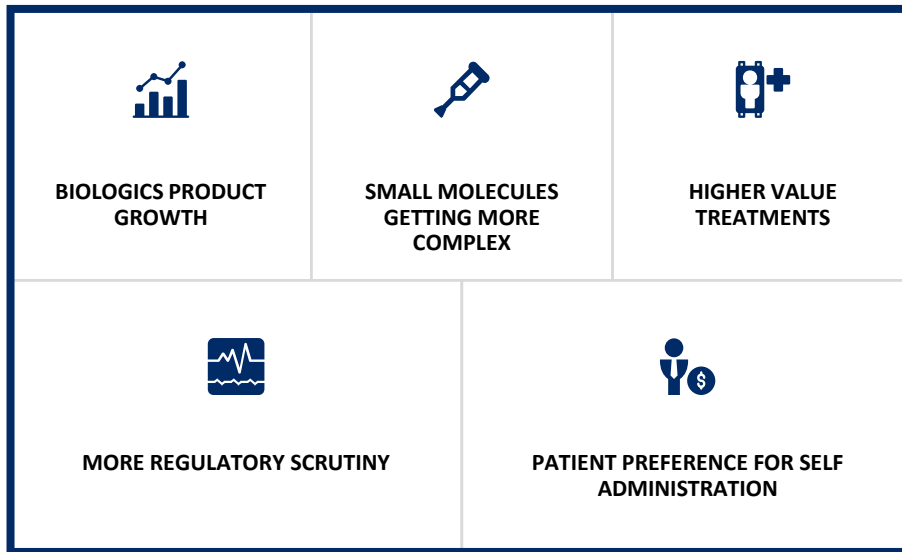
\$1.1 million
lost sales for each day a
drug's development and
launch is delayed¹

¹ Based on data from Tufts Center for the Study of Drug Development

² Biopharmaceutical Research & Development: The Process Behind New Medicines.

³ Biotechnology Innovation Organization: Clinical Development Success Rates

Global Injectable Trends Affecting Packaging



OUTCOMES:

HIGHER COST & GREATER RISK ASSOCIATED WITH FAILURE

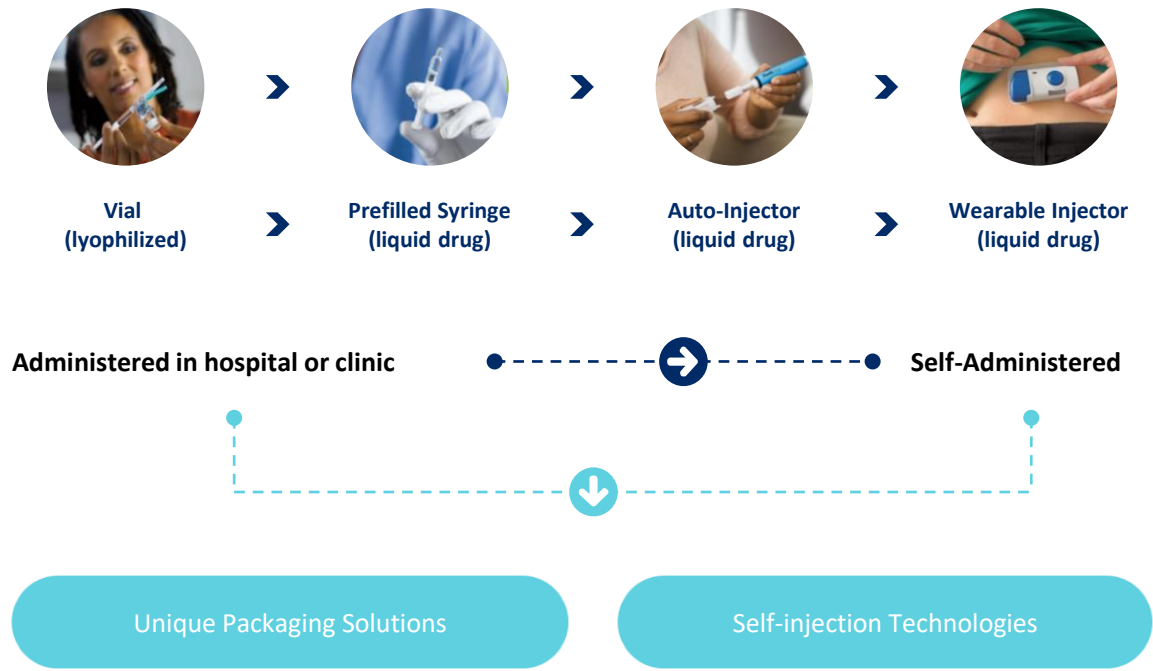
INCREASED EXPECTATIONS OF PACKAGING



What Do Changing Patient Dynamics Mean for Drug Administration?

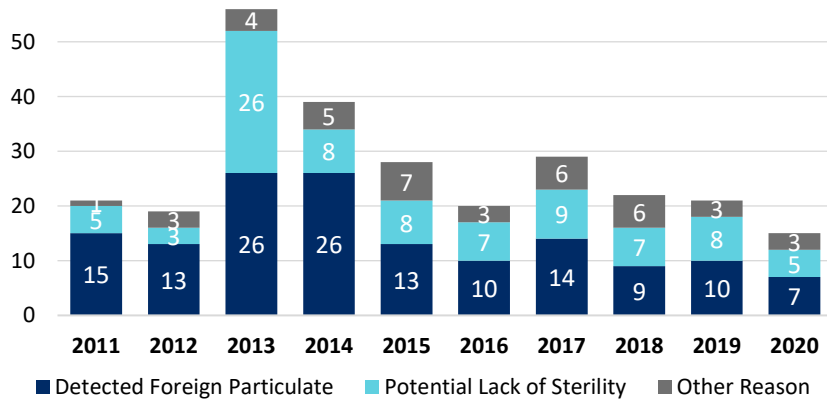
Patient Dynamics

- More chronic diseases
- Patient choice & compliance
- Home administration
- Digitalized application solutions



Particulates and Lack of Sterility Cause Most Product Recalls

Reason For Injectable Product Recalls¹



85% of recalls due to particulate and lack of sterility



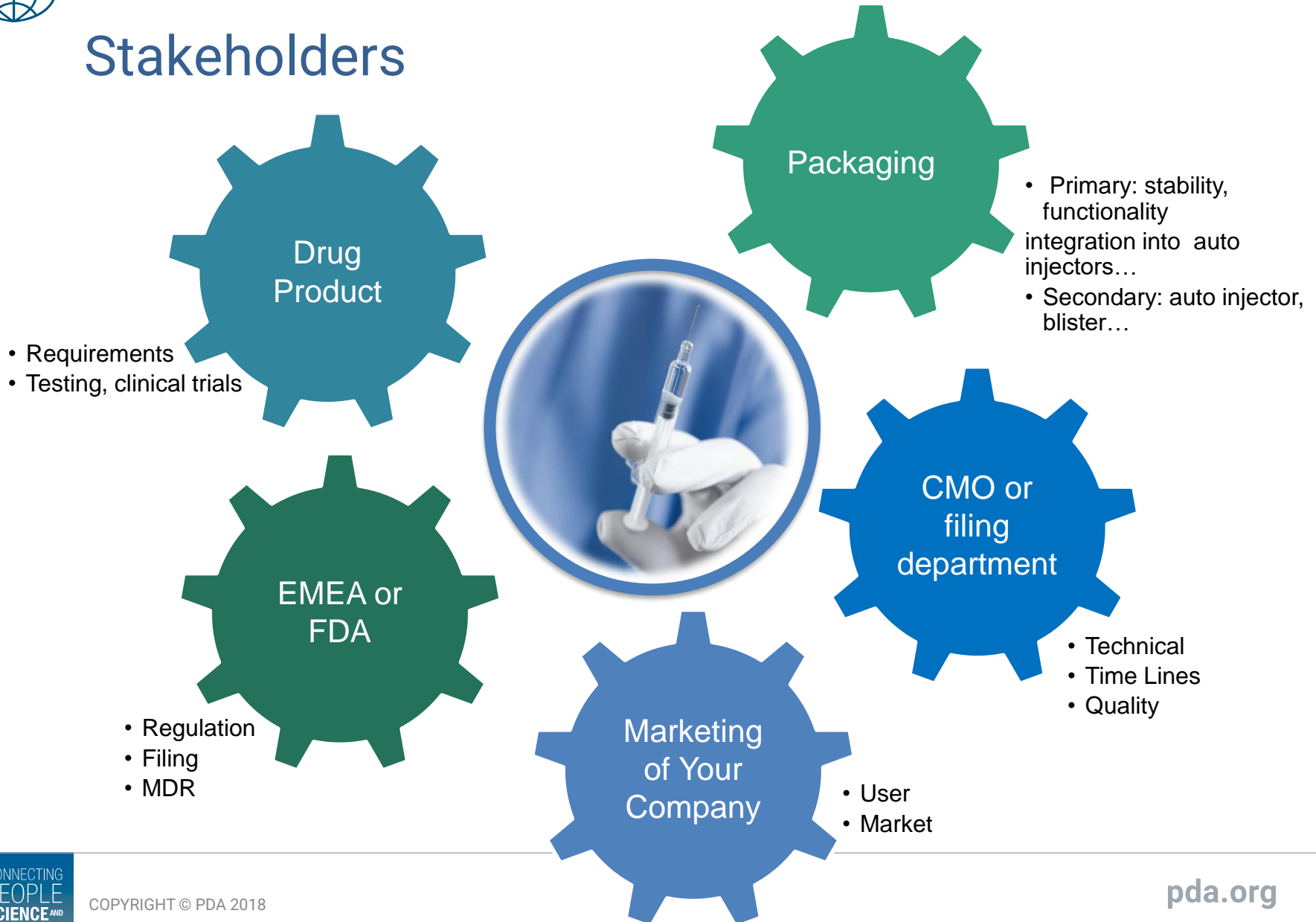
Regulatory agencies driving for better product quality

1. Source FDA

Diverse Syringes for Diverging Needs

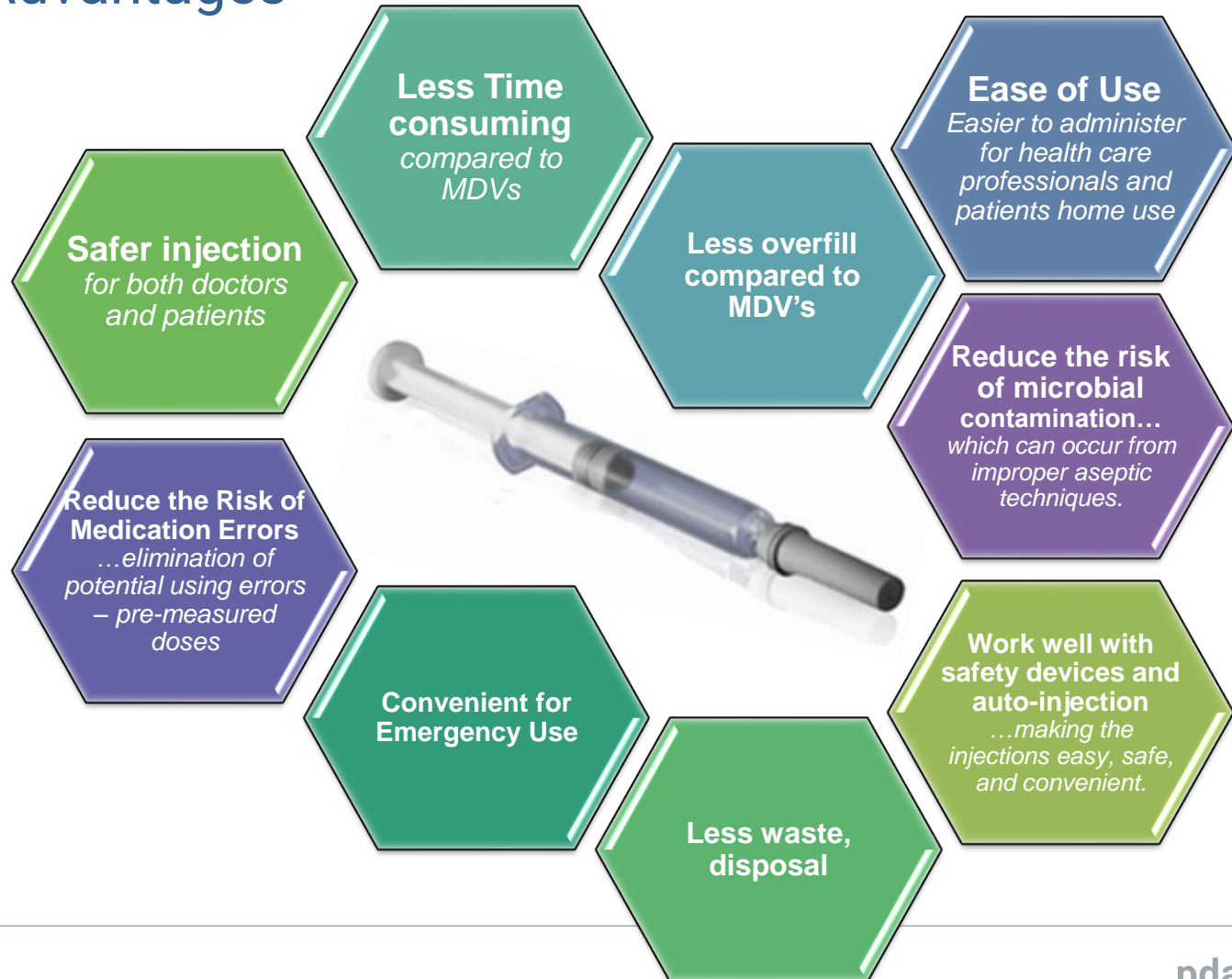
	Heparins - anticoagulants	Vaccines – mainly flu vaccines, also Covid	Biologics – very diverse group	Aesthetics – beauty and lifestyle
Injection mode	Subcutaneous injection, 1/2” needle	Intramuscular injection, 5/8” needle	Mostly subcutaneous injection, 1/2” needle	Subcutaneous injection, diverse needles SC, ID
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 Disposable needle	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: Ophthalmic luer lock, dose mark, particles	Hyaluronic acid not oxygen sensitive

Stakeholders



Multi Dose Vials MDV's - Prefilled Syringes

Some Advantages

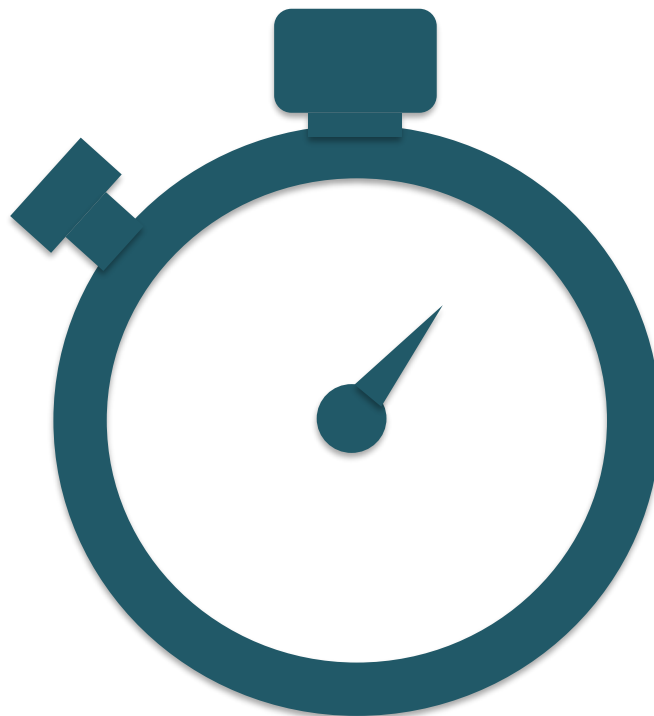


Convenience / Ease of Use / Patient Satisfaction (e.g. Copaxone[®])



Preparing injection for
COPAXONE[®] filled in a vial

235 sec.



Preparing injection for
COPAXONE[®] filled in PFS

38 sec.

A typical patient is able to save about **20h a year** by using
Copaxone[®] in a PFS format

Copaxone[®] 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



Decision making – does a syringe make sense? User vs. Payer perspective

Basic market share:

Safety first

Where is the point of care (who is the user):

Convenience for patient or hcp:
Hospital (hcp- health care professional)? *Vial ok*
Home use (patient)? *Syringe better*

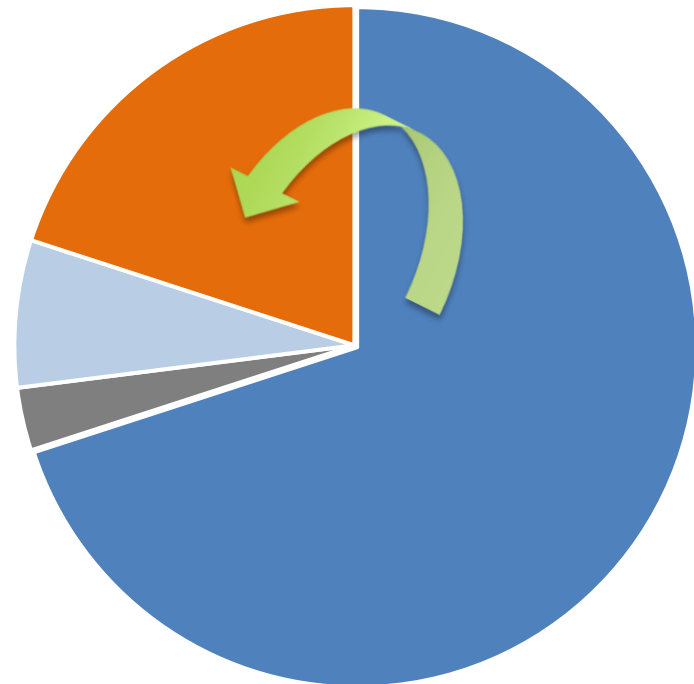
What is most economic? Vial or syringe better?

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

Drug fomulation possible in syringe?

Life cycle management from vial to syringe

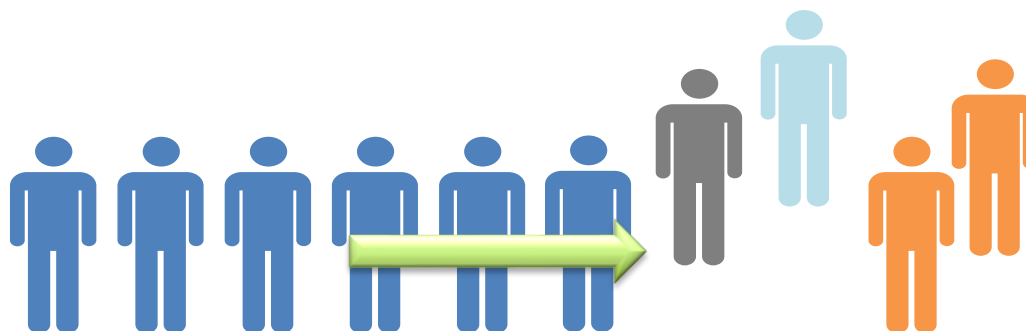
- Infusion vial
- Wearable
- Autoinjector - PFS inside
- PFS (w and w/o safety system)



Decision making – does a syringe make sense?

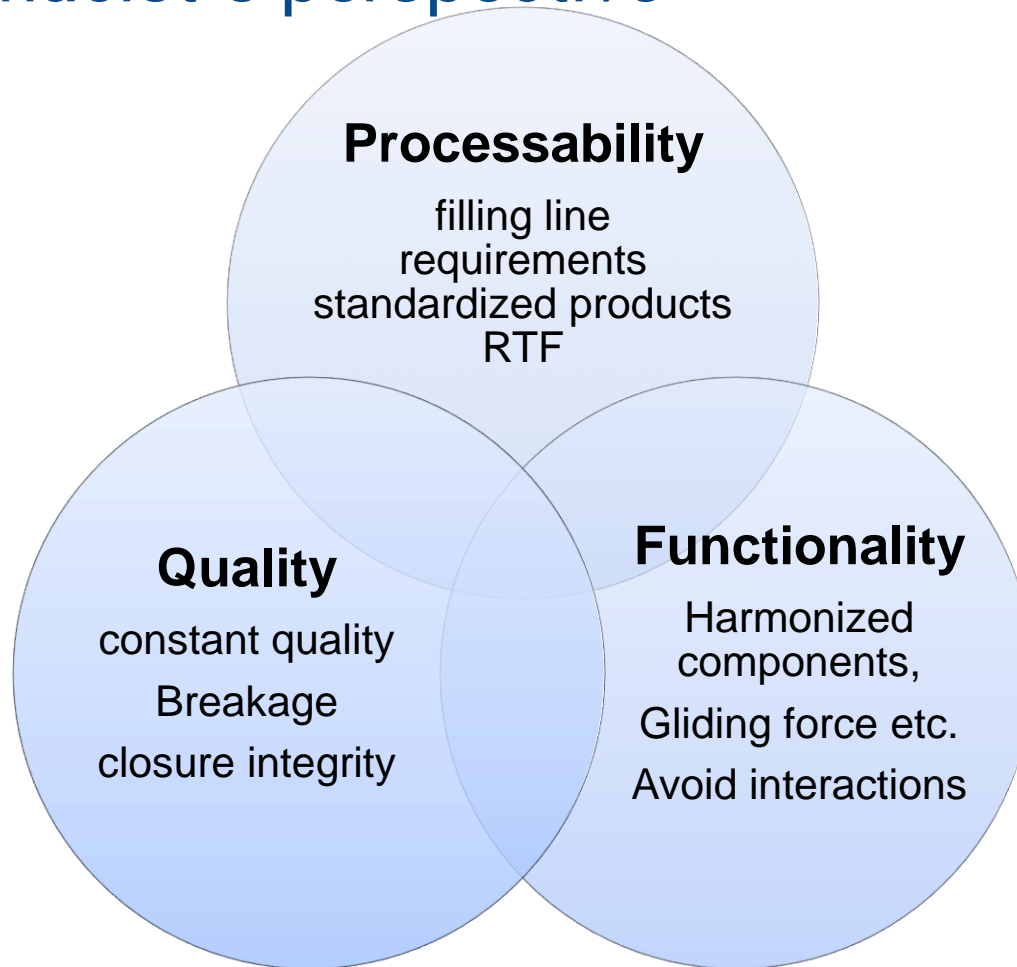
Prefilled Glass Syringe	Advantage	Filled Glass Vial	Advantage
Overall cost of container		Overall cost of container	
Low overfill, low residual volume	↑	High overfill, higher residual volume	↓
Higher cost of prim pack	↓	Low cost of vial itself	↑
User friedliness		User friedliness	
Single dose	↑	Multi dose	↓
Few steps before injection	↑	More steps before injection	↓
Low risk off false dosing	↑	Higher risk of false dosing	↓
No additional components (staked-in needle) needed at point of care Exception: disposable cannula in case of Luer syringes	↑	Disposable components needed at point of care: plastic syringe to draw from vial cannula to draw from vial cannula to inject	↓
Contact materials		Contact materials	
Contact materials to formulation during storage: glass elastomer cap elastomer plunger extractable tungsten Silicone oil (lubricant) Needle glue, steel cannula	↓	Contact materials to formulation during storage: glass elastomer stopper	↑
Specialized usage		Specialized usage	
Viscous Liquid, low volume	↑	Viscous Liquid	↓
Lyophilization, reconstitution	↓	Lyophilization, reconstitution	↑
Autoinjector, ease of use, home use	↑		↓
Overall advantage	7↑3↓	Overall advantage	3↑7↓

Decision making – does a syringe make sense?



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

Requirements towards primary containers Pharmacist's perspective



Requirements towards Injections and Ophthalmics

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