All about Pre-filled Syringe Systems

From Initial Development to Final Fill Finish

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Venice, April 20st 2023 – DAY 1

PDA Parenteral Drug Association

West

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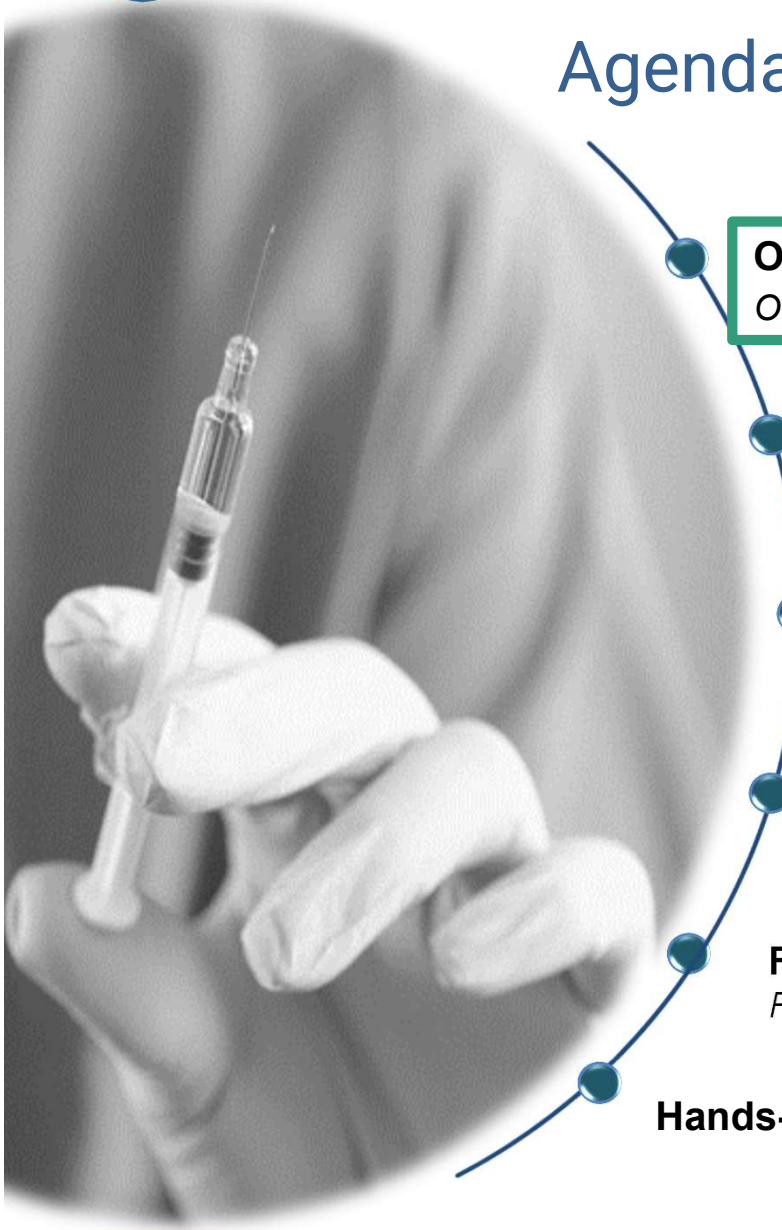


Agenda – DAY 1

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

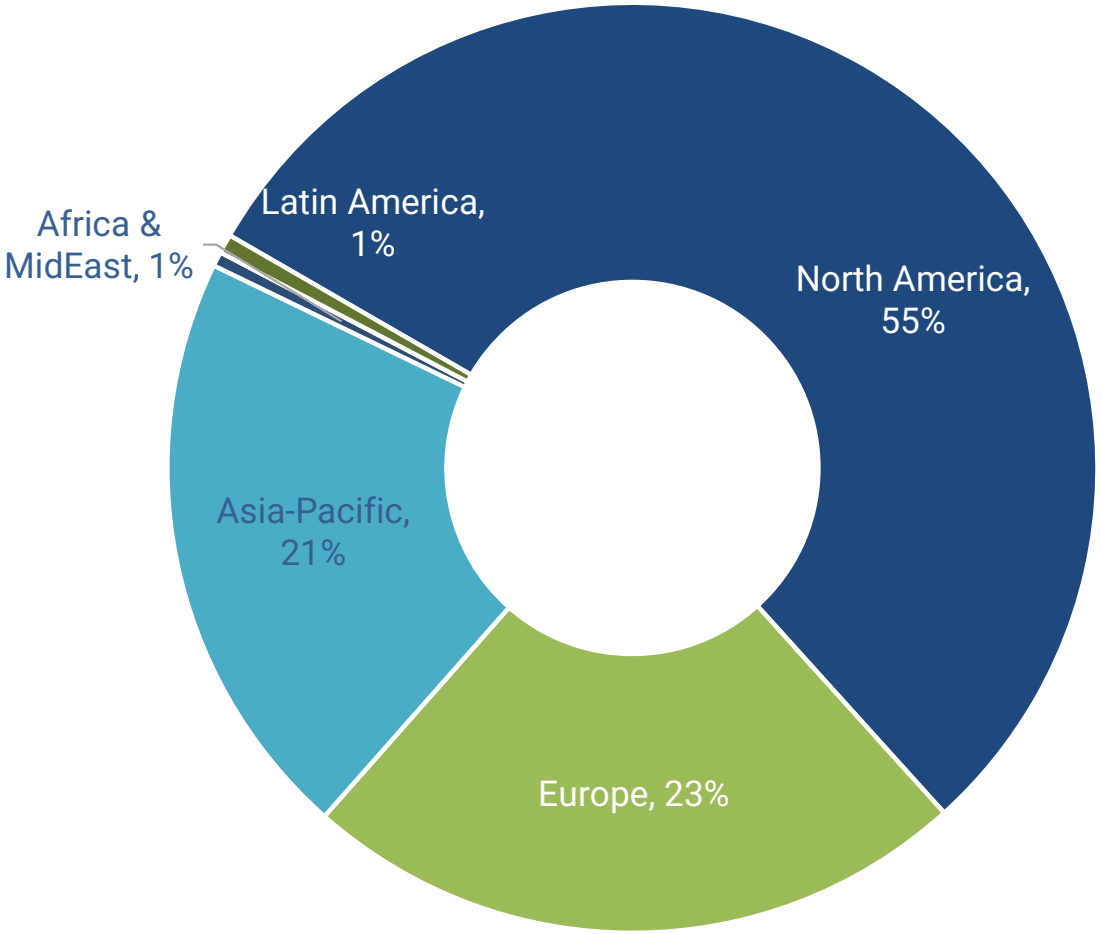
- Elastomeric Components:
- Lyophilization or Serum Stoppers

Syringe Market Overview

Global Syringe Market

- **Disposable Syringes**
  (most polypropylene)
  Drug is transferred from primary container (vial)
- **Prefillable Syringes (PFS)**
  Drug is stored in the syringe and also administered
  - **COP / COC PFS**
    Cyclic Olefin Polymer/Copolymer
  - **Glass PFS**

Injectable Value Share By Region, 2021

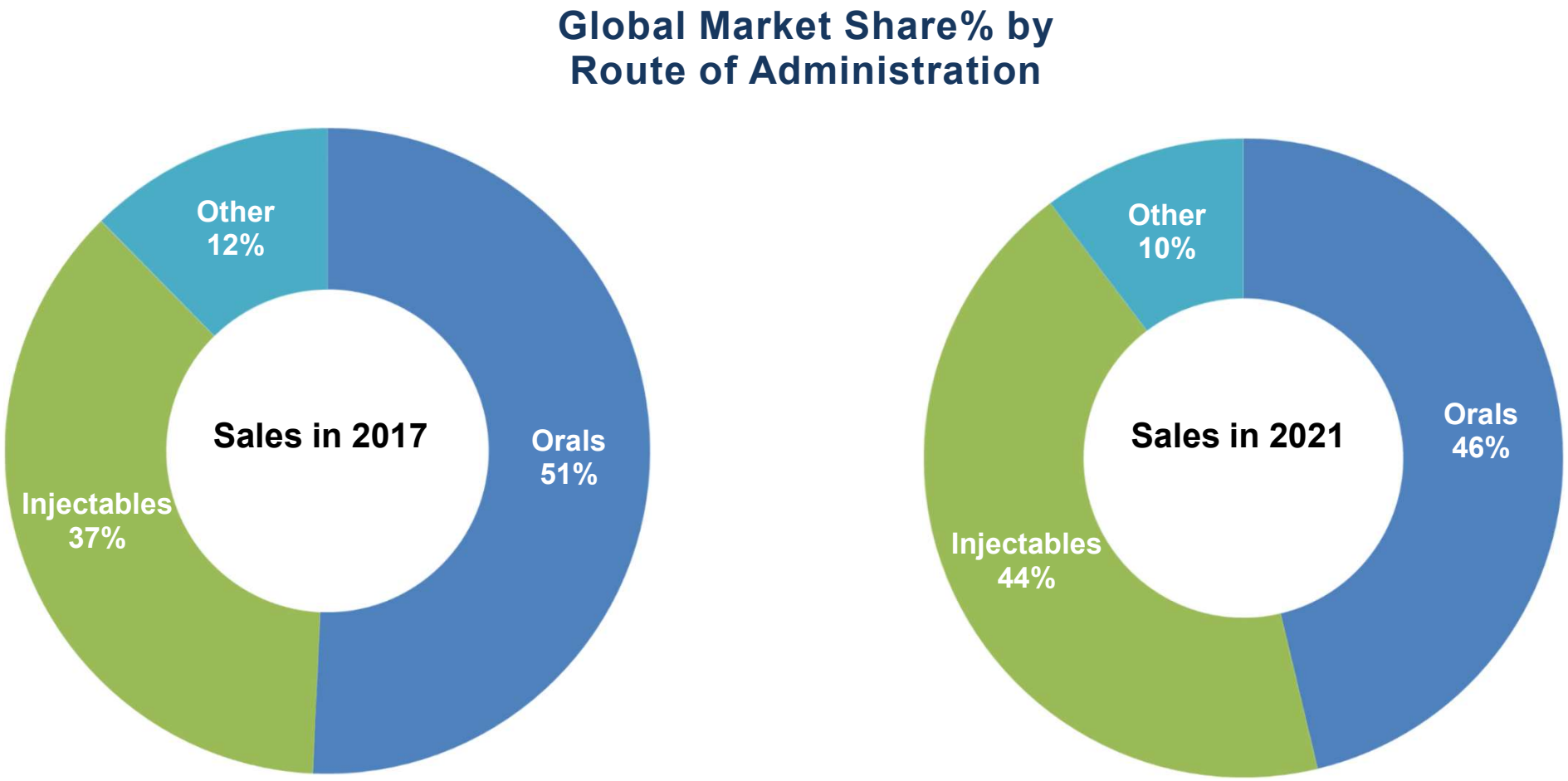


Regions	2017 - 21 CAGR
Global	10%
North America	11%
Europe	10%
Asia-Pacific	7%
Africa & MidEast	10.5%
Latin America	-4%

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

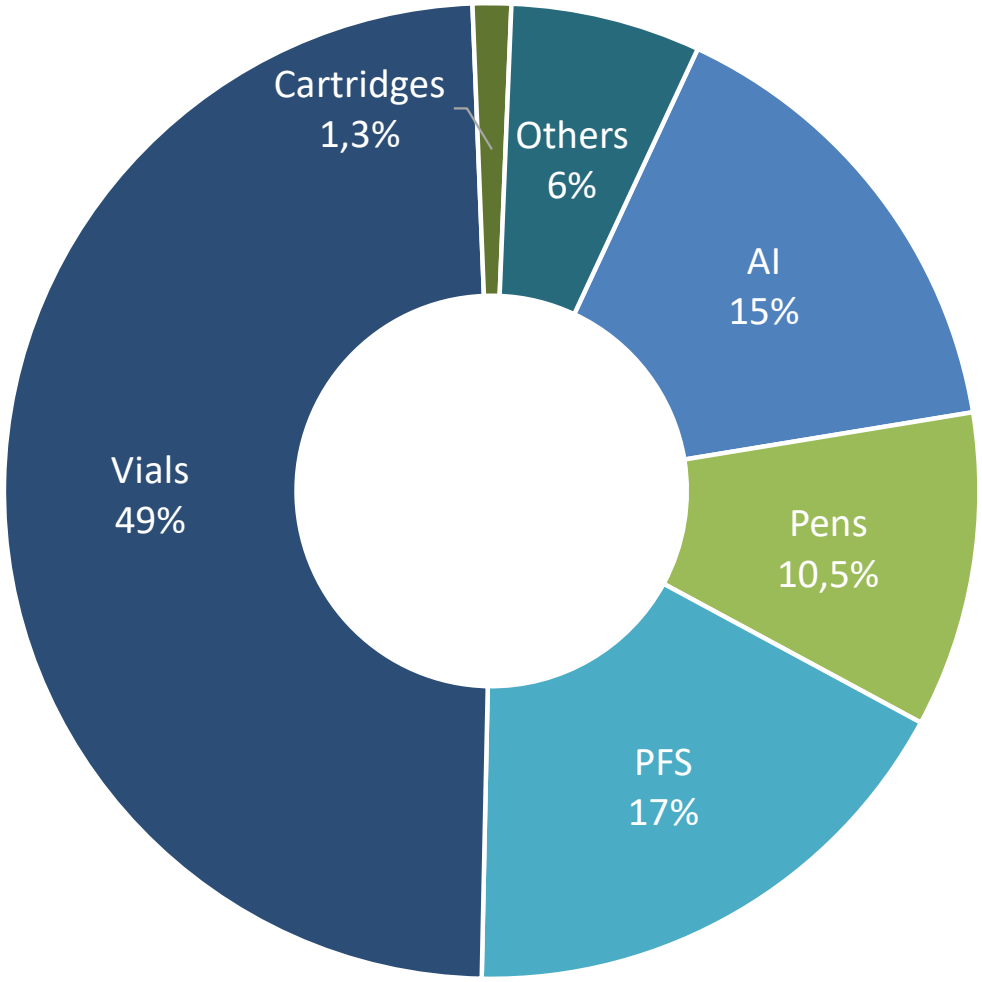
Source: IQVIA 2021 Global Audited Sales

Share of Injectables is expected to increase through 2021



Source: IQVIA 2021 Global Audited Sales

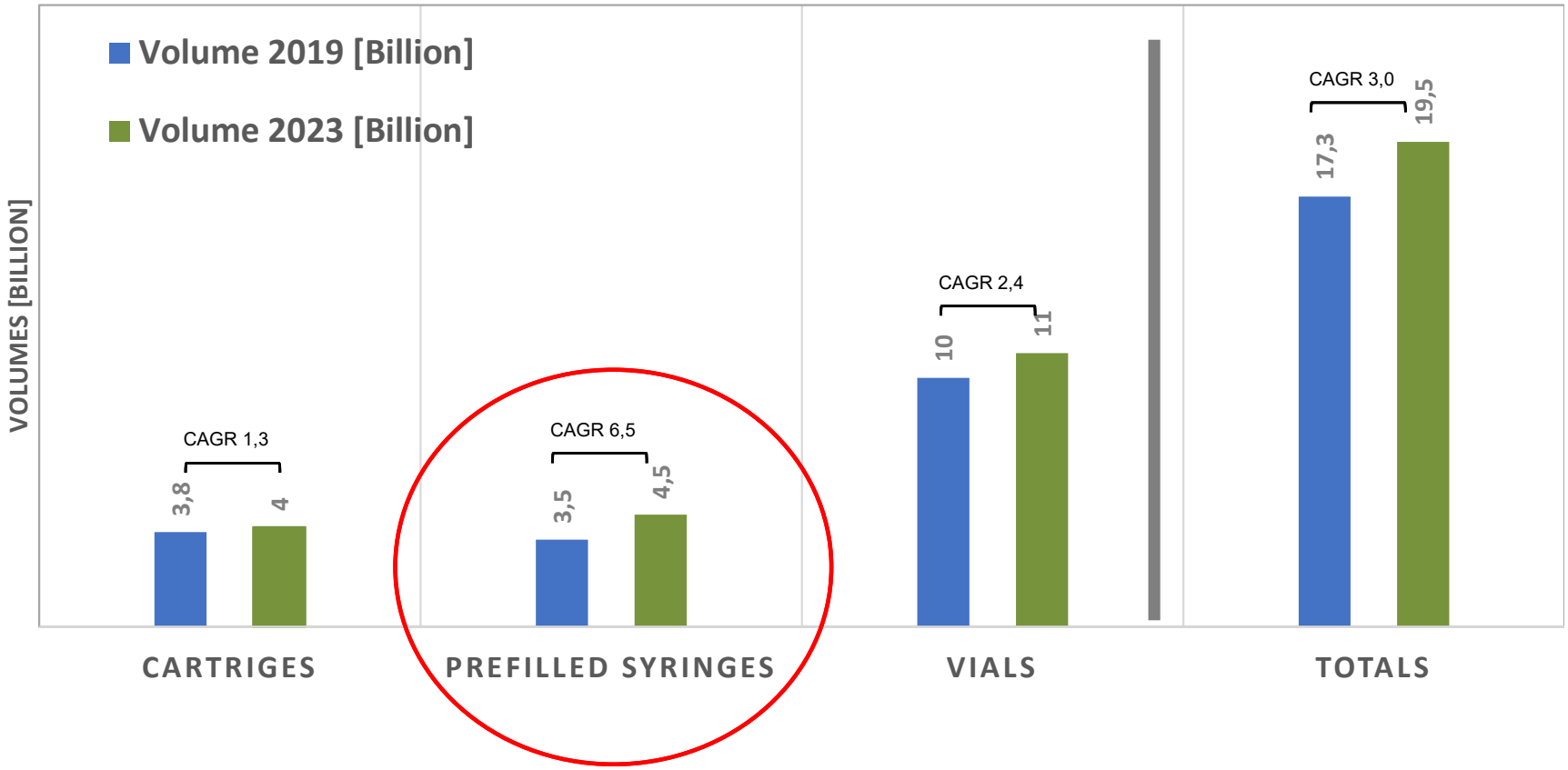
Global Injectable Value Share By Format, 2021



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

Source: IQVIA 2021 Global Audited Sales

Global Market for Parenteral Containers using Tubular Glass in Volume

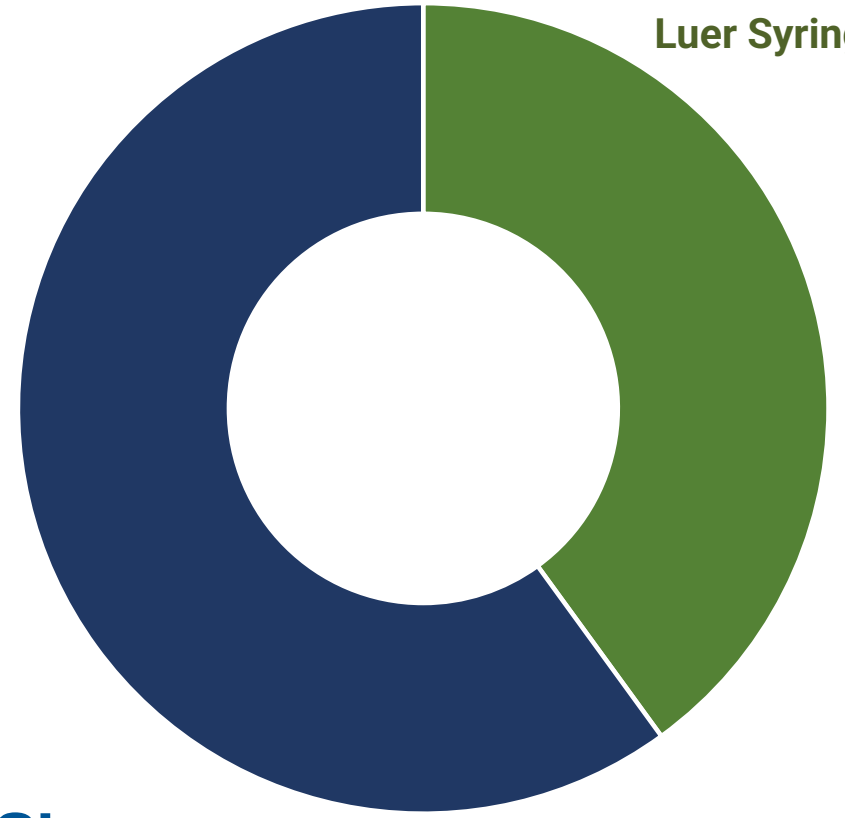


Source: ISPE Discussion Paper: Unique ID on Primary Containers to Drive Product Traceability and Quality – Feb 2021 – Stevanato Groupe

Global Prefillable Syringes: 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 Rigid Needle Shields

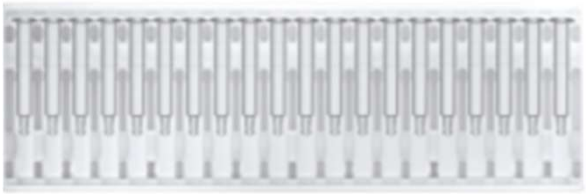


Source: Internal data on file with West

Global Prefilled Syringe Bulk vs Ready-to-Use

Ready-to-Use Nested glass syringes in tubs

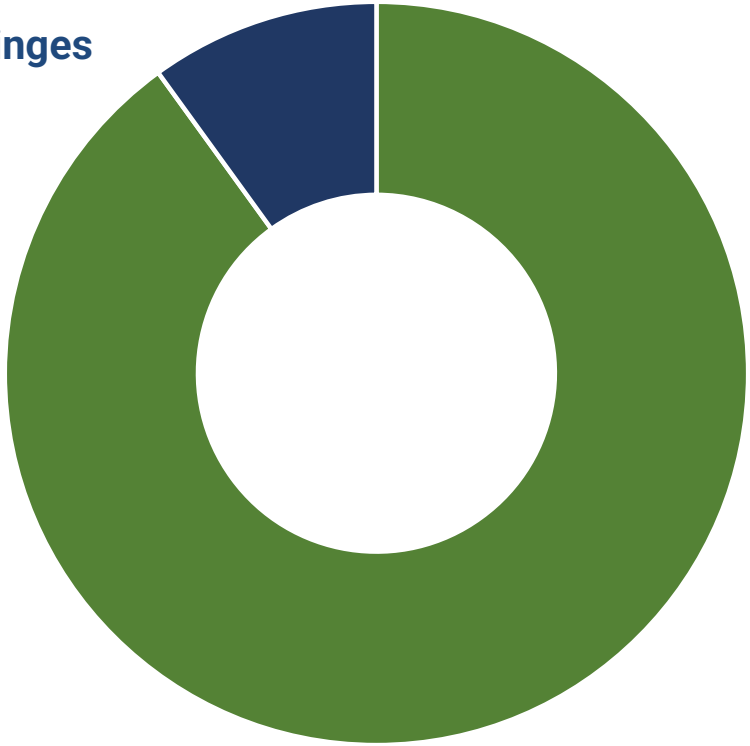
Pictures property to Gerresheimer



Bulk glass syringes on rondo trays

Share 10%

Bulk Syringes



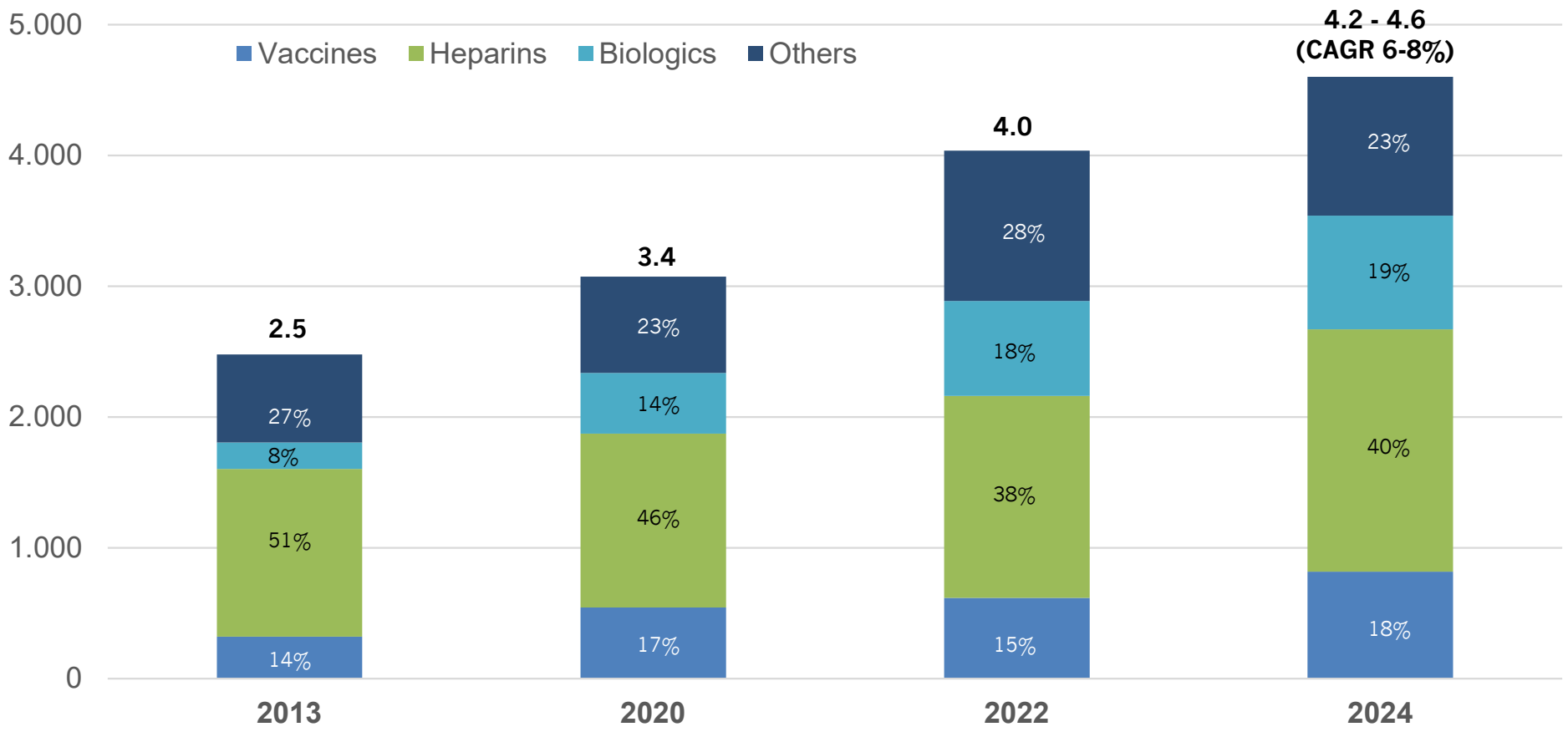
Share 90%

Ready-to-Use syringes

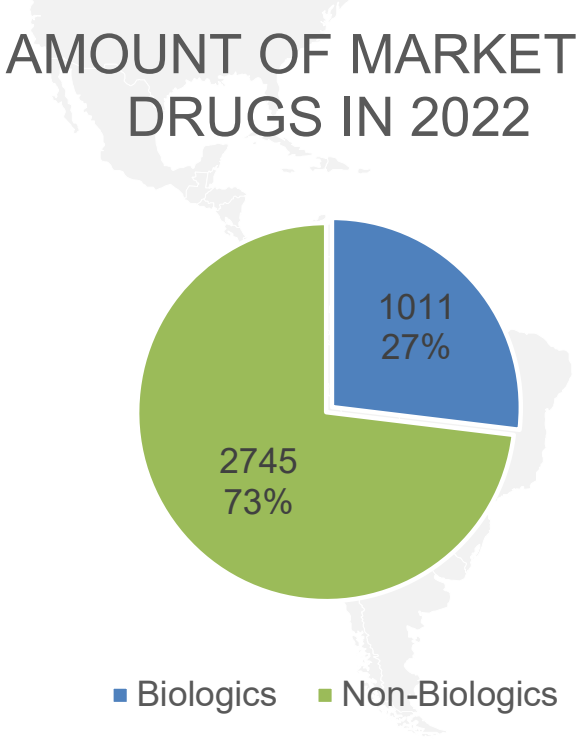
Source: Internal data on file with West

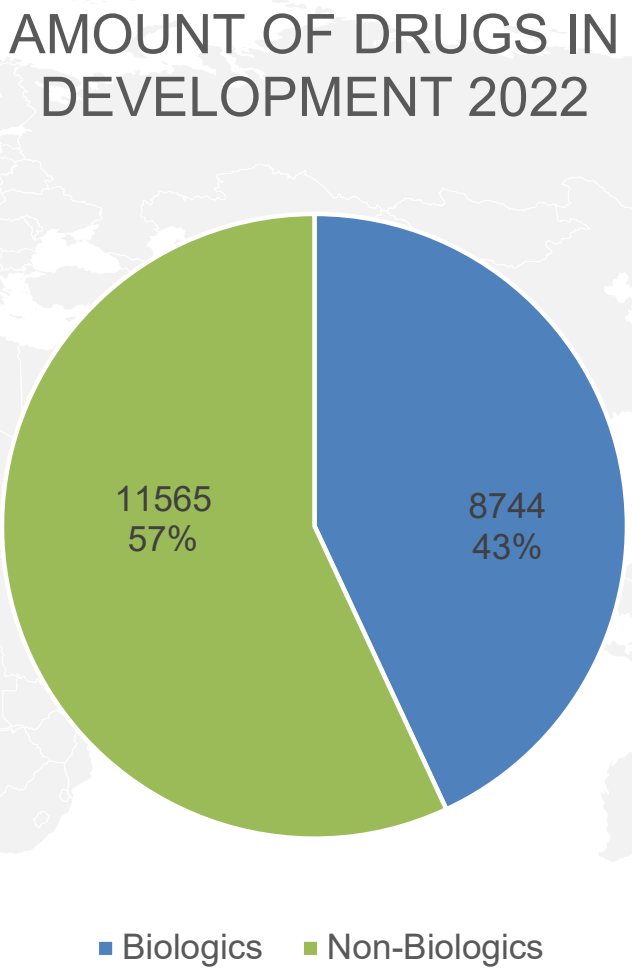
Syringe market demand per indication

Global syringe market [IQVIA and internal estimation] - average CAGR [bpcs.]

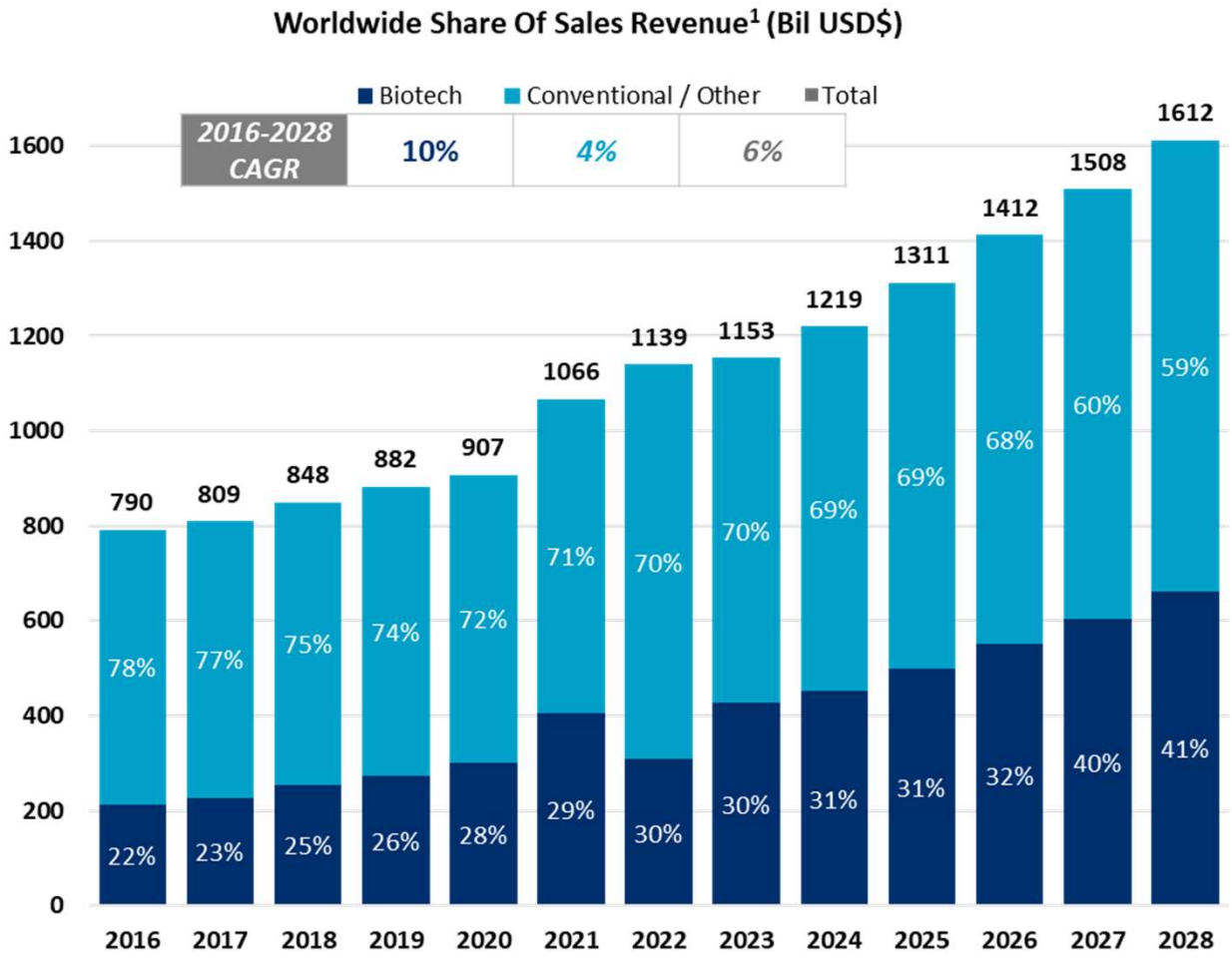


Biologic / Non-Biologic market total in 2022





Biologics Continue to Drive Pharmaceutical Value Growth

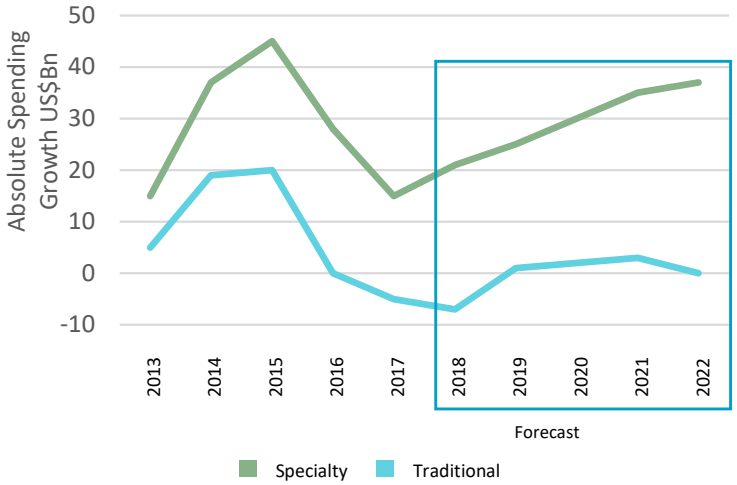


- Biologics will grow from 22% to over 41% of global spend (2016-2028)
- Revenues from biologics are forecasted to reach $661 billion by 2028[1]

Source: 1. Evaluate Pharma - World Preview 2022, Outlook To 2022: Patents and Pricing

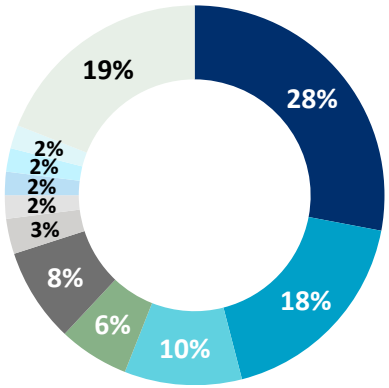
Specialty Medicines will Drive all Spending Growth in Developed Markets

Brand Spending Growth of Specialty & Traditional Drugs 2018-2022 in Developed Markets[1]

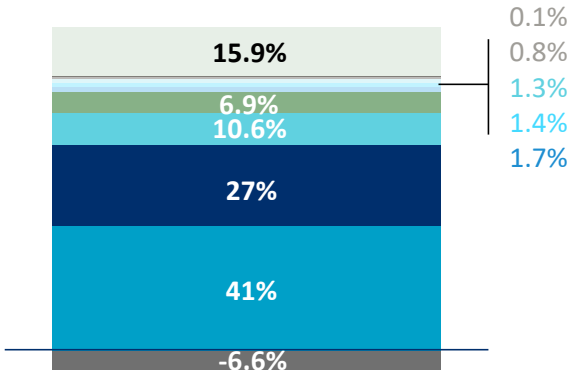


Specialty Medicines Spending & Growth in Developed Markets[2]

Share of 2017 Developed Markets Specialty Spending $297Bn



Developed Markets Specialty Spending Growth 2018-2022, $140-150Bn



Oncology | Autoimmune | HIV | Immunosuppressants | Antivirals | GM-CSF
ESA | AMD | Blood Coagulation | Poly IVIG IV/IM | Others

Implications

Smaller patient populations	→ Need for smaller production batches	→ Emergence of precision medicine
Increased sophistication and sensitivity of drugs	→ Higher costs per dose	→ Focus on patient safety and outcomes to justify higher costs

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Source: [1]IQVIA Institute, Oct 2017. Notes: Developed markets include U.S., Japan, Germany, France, Italy, U.K., Spain, Canada, S.Korea, Australia. [2]IQVIA Institute, Oct 2017. GM-CSF = Granulocyte-macrophage colony-stimulating factor; ESA = Erythropoiesis-stimulating agents; AMD = Age-related macular degeneration.

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[1]

Drug development takes a long time

It takes an average of

over 10 years

from first patent filing to market[2]

Drug development is increasingly risky

Only 10%

of drugs entering clinical testing receive regulatory approval[3]

Impact of Delays

$1.1 million

lost sales for each day a drug's development and launch is delayed[1]

[1] Based on data from Tufts Center for the Study of Drug Development
[2] Emerging Biopharma's Contribution to Innovation, June 2022, IQVIA.
[3] Biotechnology Innovation Organization: Clinical Development Success Rates

Our Healthcare Industry is Evolving

1. **Increase in Emerging Company Development**

   +1700 new pipeline molecules from emerging companies 2016-21.

2. **Trend to Self-Administration / Combination Products**

   49% Of injectables in market can be self-administered, led by PFS, Auto Injector

3. **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.

4. **Increased Connectivity Prevalence and Awareness**

   McKinsey projects $420B in healthcare efficiency gains from connected health by 2030

5. **Increased Focus on Sustainability**

   Customers and competitors investing in sustainable packaging, social responsibility efforts, and environmental actions

6. **Regulatory Complexity is Increasing**

   Driven by combination products, accelerated reviews, and China improved quality expectations

7. **RNA and Cell/Gene Therapy Significantly Rising**

   +20% pipeline CAGR, 600 new pipeline molecules 2016-2021

8. **Covid Creates More Focus on Supply Chain Resiliency**

   Enormous stress on all areas of the Global supply chain leading to government and industry investment

What Do Changing Patient Dynamics Mean for Drug Administration?

Patient Dynamics

More chronic diseases

Patient choice & compliance

Vial
(liquid or lyophilized)

Prefilled Syringe
(liquid drug)

Self/Auto-Injector
(liquid drug)

Wearable Injector
(liquid drug)

Home administration

Administered in hospital or clinic → **Self-Administered**

Digitalized application solutions

Unique Packaging Solutions

Self-injection Technologies

Important SmartDose and SelfDose product and safety information and warnings available at: https://www.westpharma.com/products/self-injection-platforms/smartdose/smartdose-3-5 and https://www.westpharma.com/products/self-injection-platforms/selfdose.

Stakeholders

Drug Product

- Requirements
- Testing, clinical trials

Packaging

- Primary: stability, functionality

integration into auto injectors…

- Secondary: auto injector, blister…

CMO or filing department

- Technical
- Time Lines
- Quality

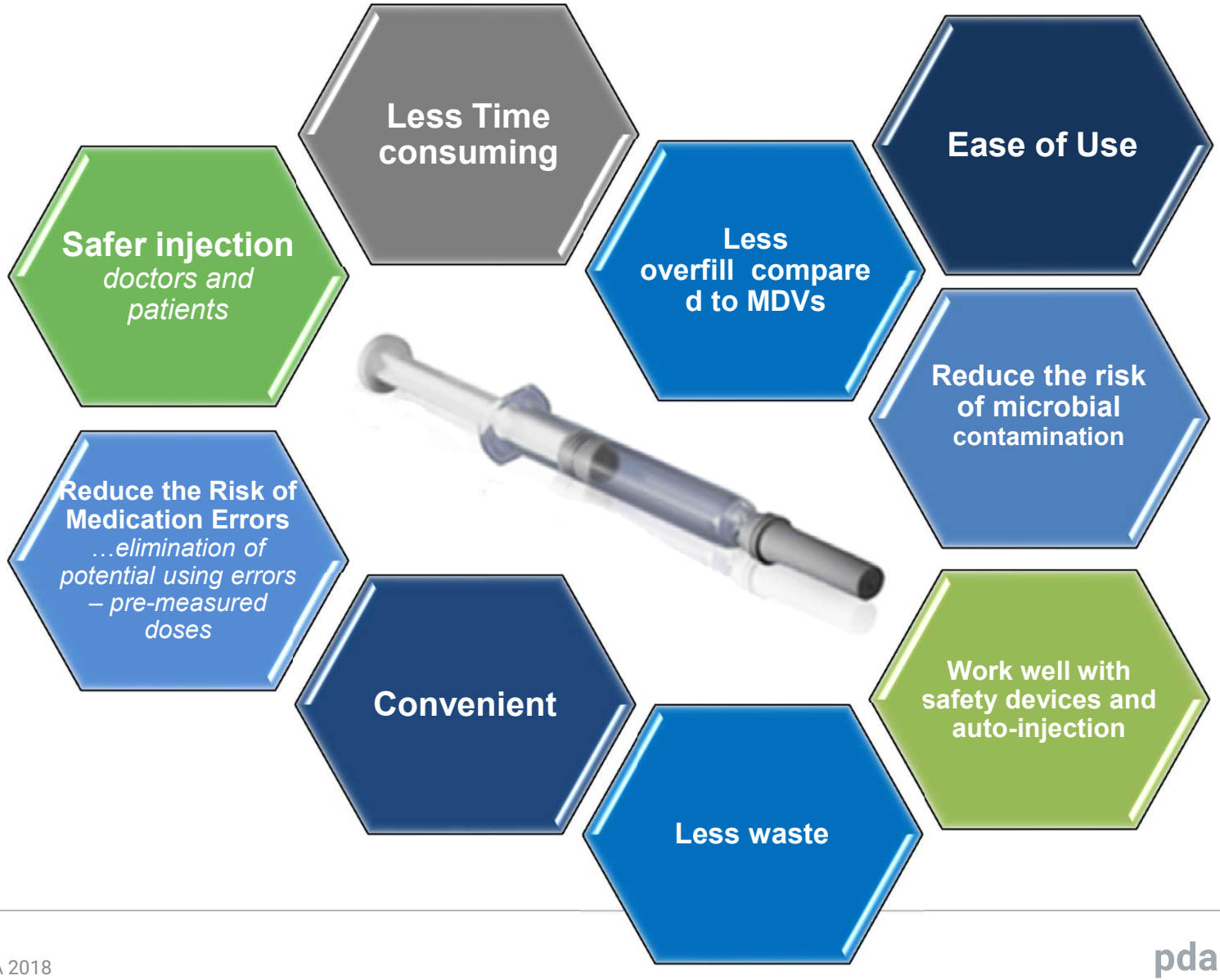
EMEA or FDA

- Regulation
- Filing
- MDR

Marketing of Your Company

- User
- Market

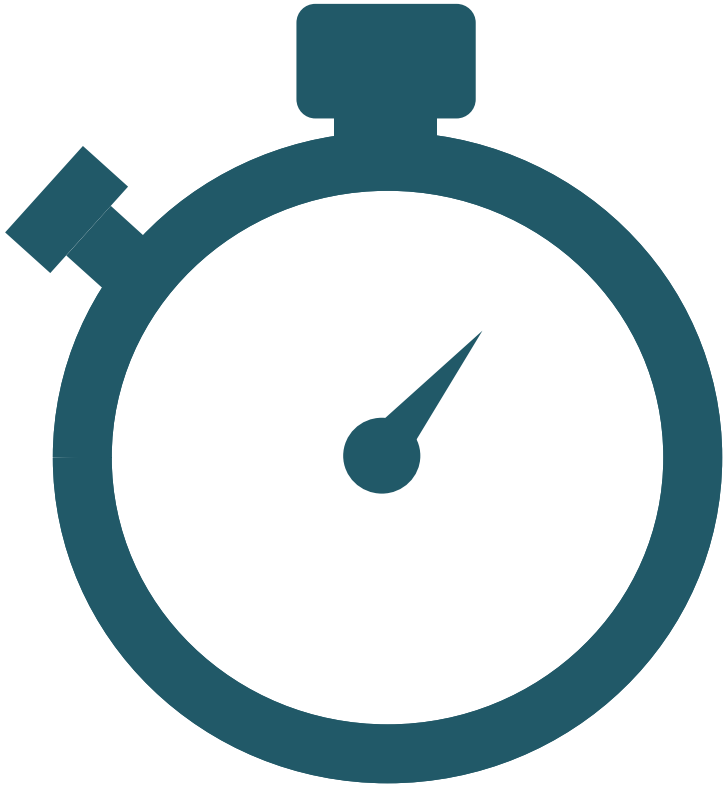
Multi Dose Vials [MDVs] - Prefilled Syringes: some advantages



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.

Source: Pharmaceutical Technology, supplement sep 2009 Issue, Author: Raul Soikes

Diverse Syringes for Diverging Needs

	Heparins - anticoagulants	Vaccines – mainly flu vaccines	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

Decision making – does a syringe make sense?

Prefilled glass syringe	Advantage	Filled glass vial, closed	Advantage
Total cost for container			
Low overfilling, low residual volume	+	High overfilling, high residual volume	–
Higher costs for packaging materials	–	Lower costs for packaging materials	+
User-friendliness			
Single dose	+	Single or multiple dose	+
Few steps through to injection	+	Many steps in injection preparation	–
Low risk of incorrect dosing	+	Higher risk of error for correct dosing	–
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	–
Contact materials			
Contact with the drug during storage: Glass Elastomer stopper Elastomer cap Tungsten (extractables) Silicone oil (glide agent) Needle adhesive, Stainless steel	–	Contact with the drug during storage: Glass Elastomer stopper	+
Special applications			
Highly viscosity drugs, low volume	+	Highly viscosity drugs	–
Lyophilization, reconstitution complex	–	Lyophilization, reconstitution simple	+
Autoinjector, simplicity, home use	+	Training necessary, especially for the uninitiated	–
Overall advantage	7 | 3		4 | 6

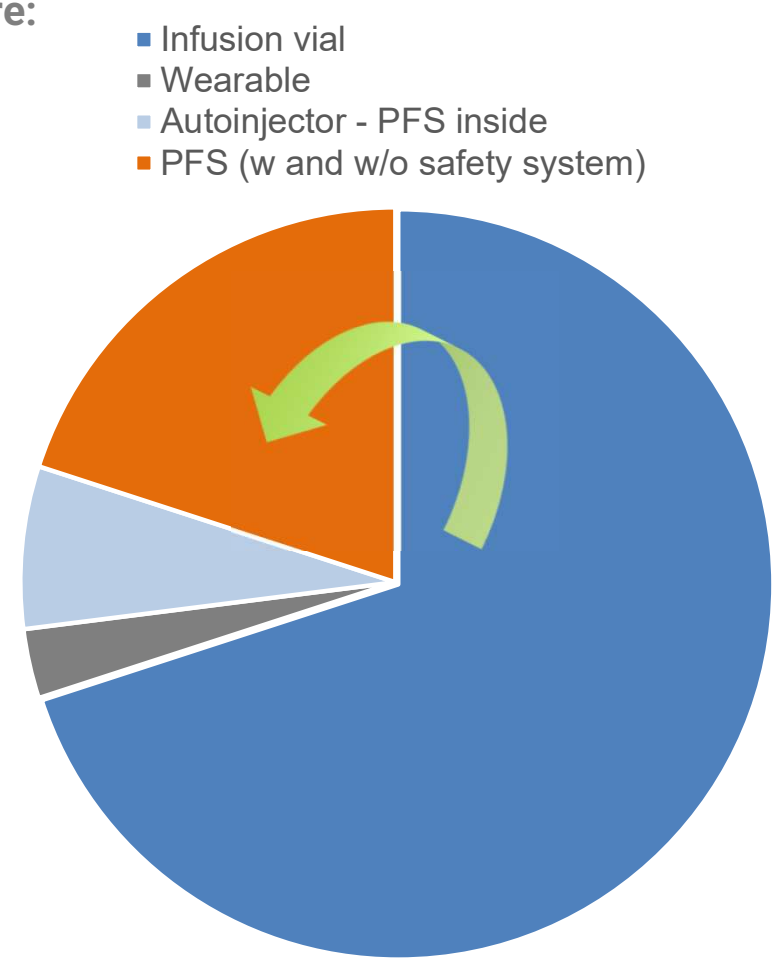
Decision making – Glass or COP?

	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
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	5 | 6	

OP = Cyclic Olefin Polymer
**EtO = Ethylene Oxide

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

Basic market share:



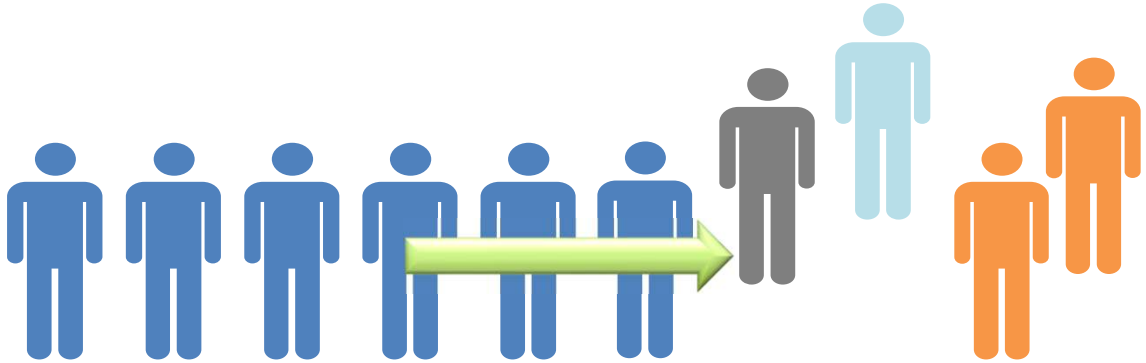
Safety first

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

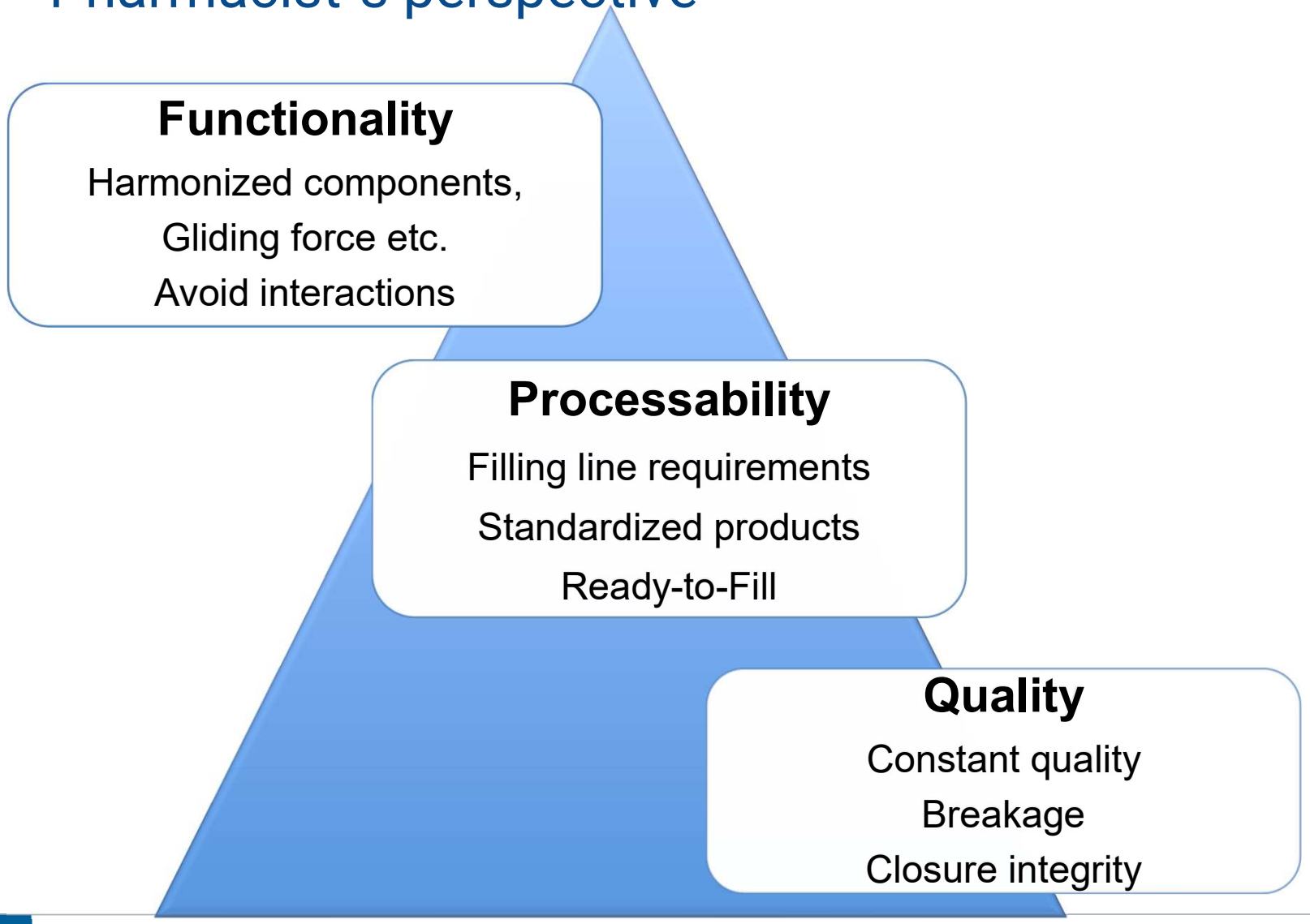
Drug formulation possible in syringe?
Life cycle management from vial to syringe

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

Thank you very much for your attention!

Any Thoughts?
Any Questions?