



# Test Methods for Prefilled Syringes

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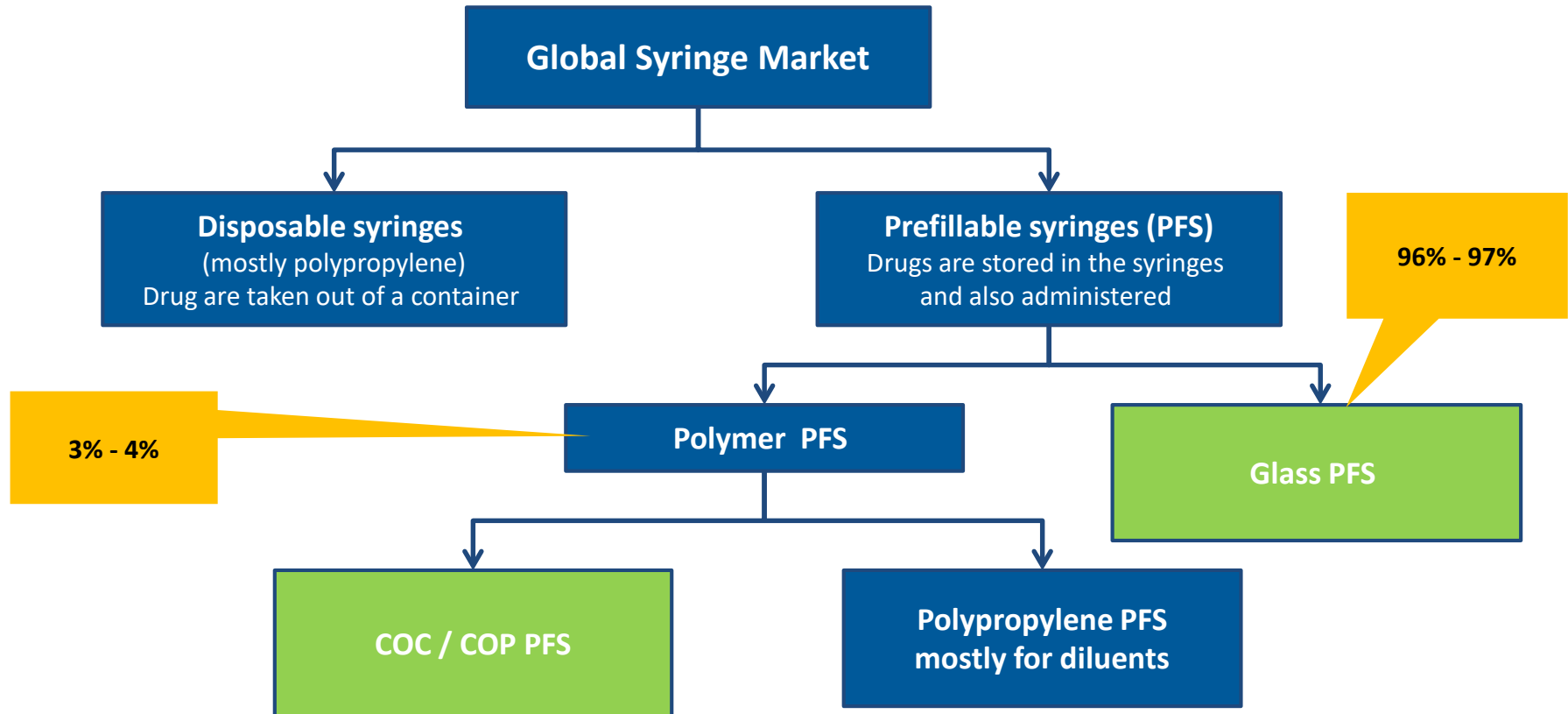
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- **Introduction to Syringe Systems & Components**



Prefilled Syringes

# Syringe Market Overview - General



**Notes:**

**COC:** Cyclic Olefin Copolymer  
**COP:** Cyclic Olefin Polymer

# Definition of Prefilled Syringes

When we are talking about syringes,  
we are talking about **Prefilled Syringes!**

## Bulk Syringes

Bulk syringes unsterile and were delivered packed in Rondo trays.



## Prefilled Syringes

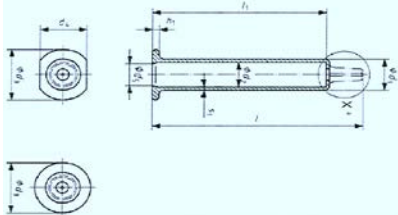
Pre-Sterilized syringes are delivered in tub and nest and are ready for filling at customers.



# Materials for Syringe Systems

Glass Formats up to 20ml,

## GLASS



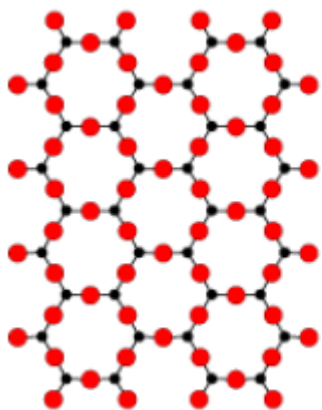
Syringe Size	OD [mm]	OD ± [mm]	ID [mm]	ID ± [mm]
0.5 ml	6.85	0.10	4.65	0.10
1ml lg	8.15	0.10	6.35	0.10
1 – 3 ml	10.85	0.10	8.65	0.20
5 ml	14.45	0.10	11.85	0.20
10 ml	17.05	0.20	14.25	0.20
20 ml	22.05	0.20	19.05	0.20

ISO 11040-4 specified Outer & Inner Diameter Dimensions



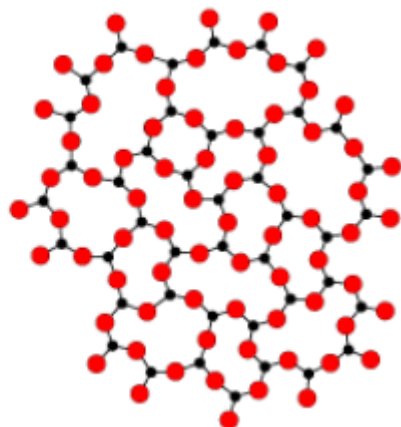
Outer Diameter: 1ml std  $9,2 \pm 0.1\text{mm}$

# Materials for Syringe Systems: Glass



Quartz crystal

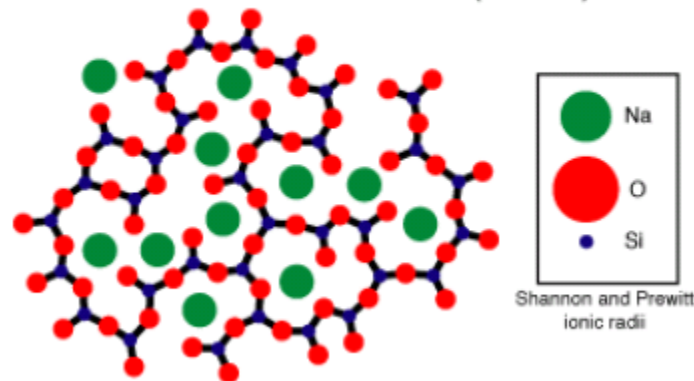
MP >2000° C



Quartz glass

MP ~1700° C

Proposed Structure of Sodium Silicate Glass  
after Warren and Bischoff (1930's)



- ❑ Mixture of crystalline oxides, carbonates, etc.
- ❑ Glass is a “frozen super cooled liquid”
- ❑ Glass is an inorganic melt, cooled down and solidified without crystallization.
- ❑ Considered solid below ~500°C, without defined melting point because of its amorphous structure.
- ❑ Composed of:
  - ❑ Network former :  $\text{SiO}_2$  ( $\text{SiO}_4^{4-}$ )
  - ❑ Network modifiers to lower melting point -  $\text{Na}_2\text{O}$ ,  $\text{B}_2\text{O}_3$ ,  $\text{PbO}$
  - ❑ Stabilizers to improve durability -  $\text{CaO}$ ,  $\text{Al}_2\text{O}_3$
  - ❑ Colorants as needed -  $\text{Fe}_2\text{O}_3$  -  $\text{TiO}_2$  & many others

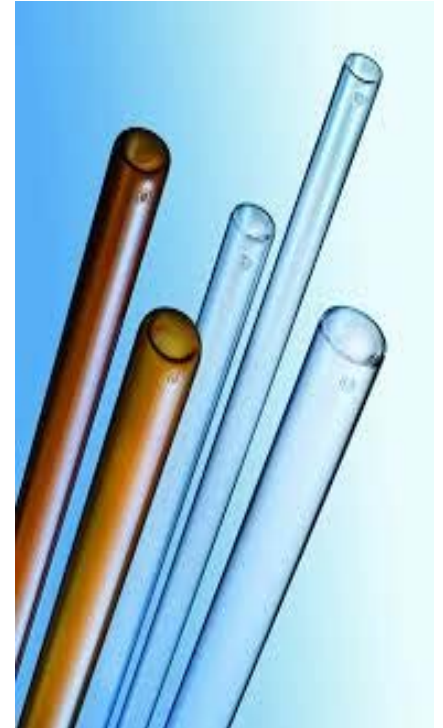
# Materials for Syringe Systems: Glass

CORNING

 **Nippon Electric Glass Co., Ltd.**

 **NIPRO**

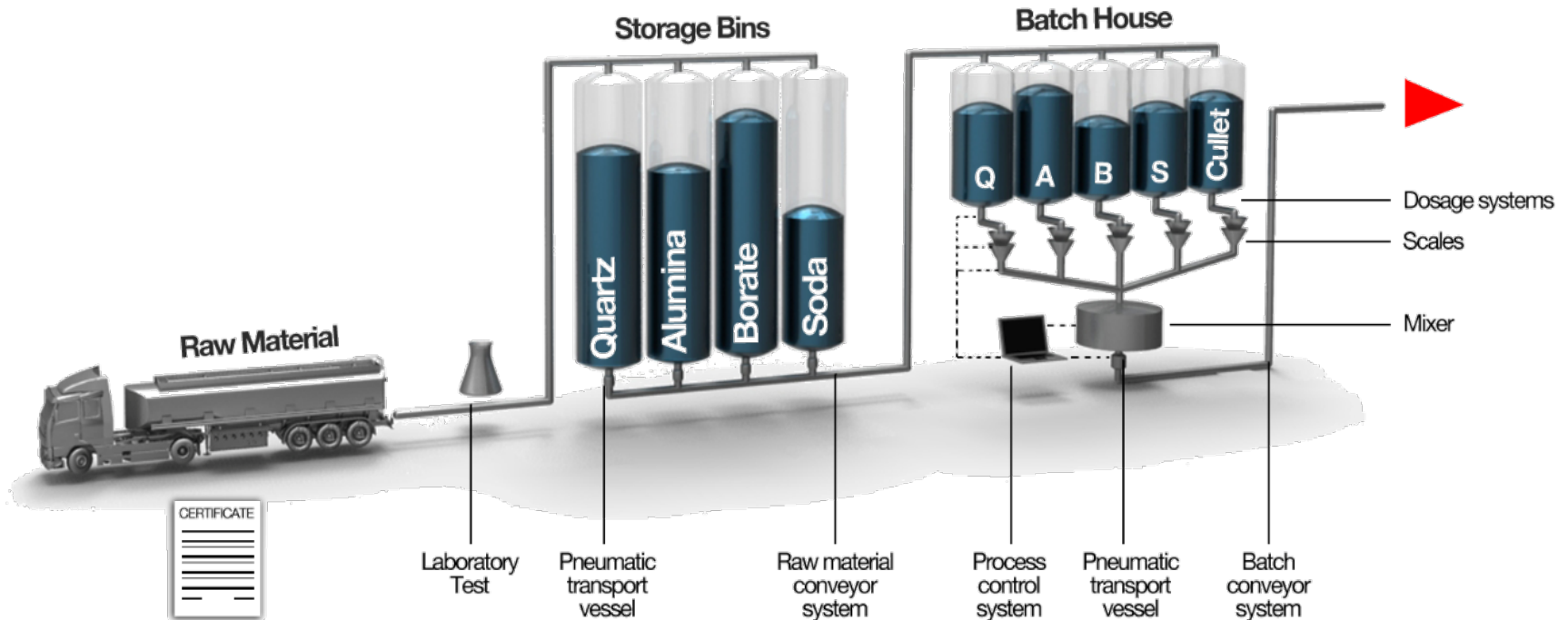
**SCHOTT**  
glass made of ideas



Non limitative list

Logos taken from companies webpages

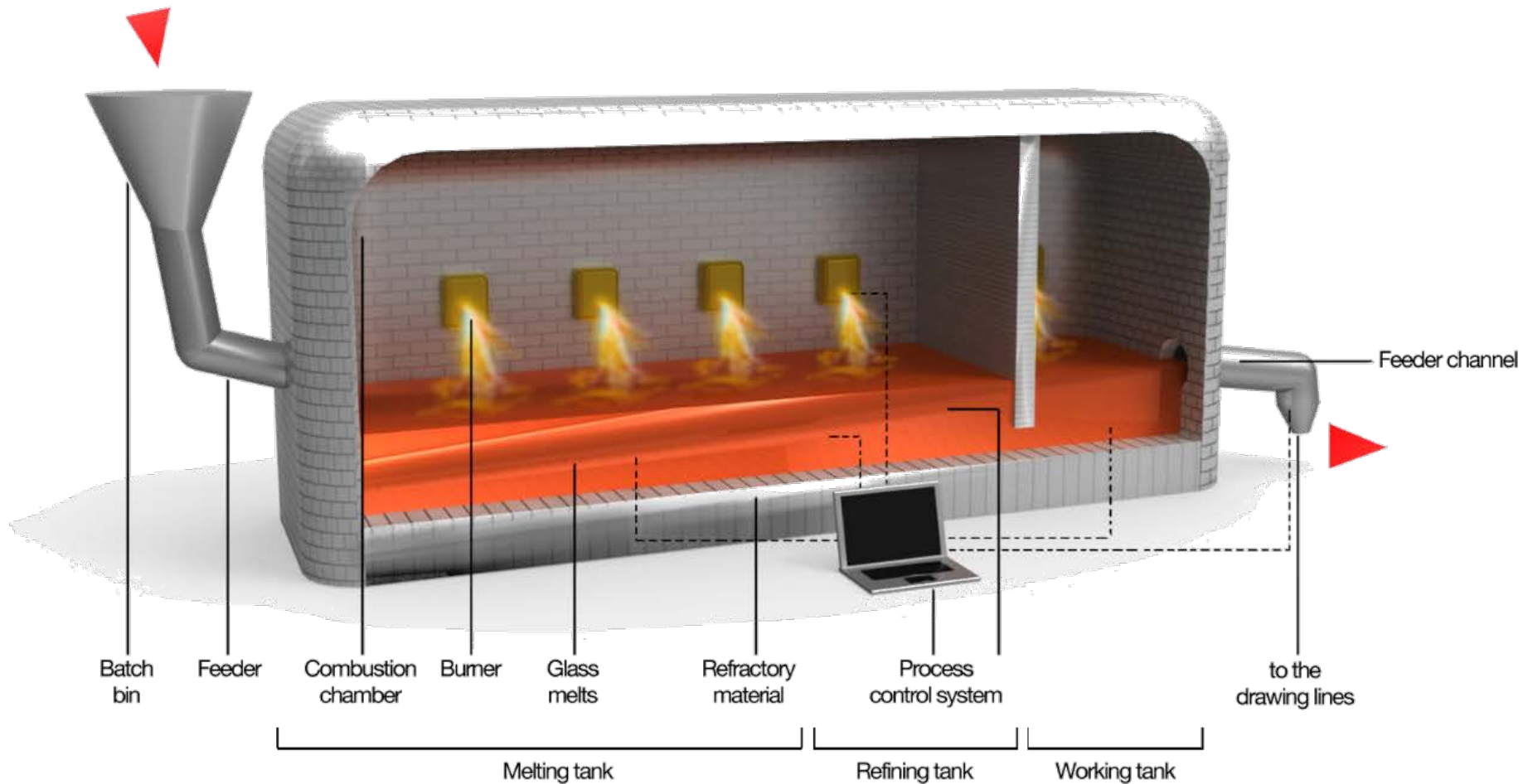
# Tubing Manufacturing Process



Graphic is courtesy of SCHOTT Pharmaceutical Systems



# Tubing Manufacturing Process



Graphic is courtesy of SCHOTT Pharmaceutical Systems

# Tubing Manufacturing Process



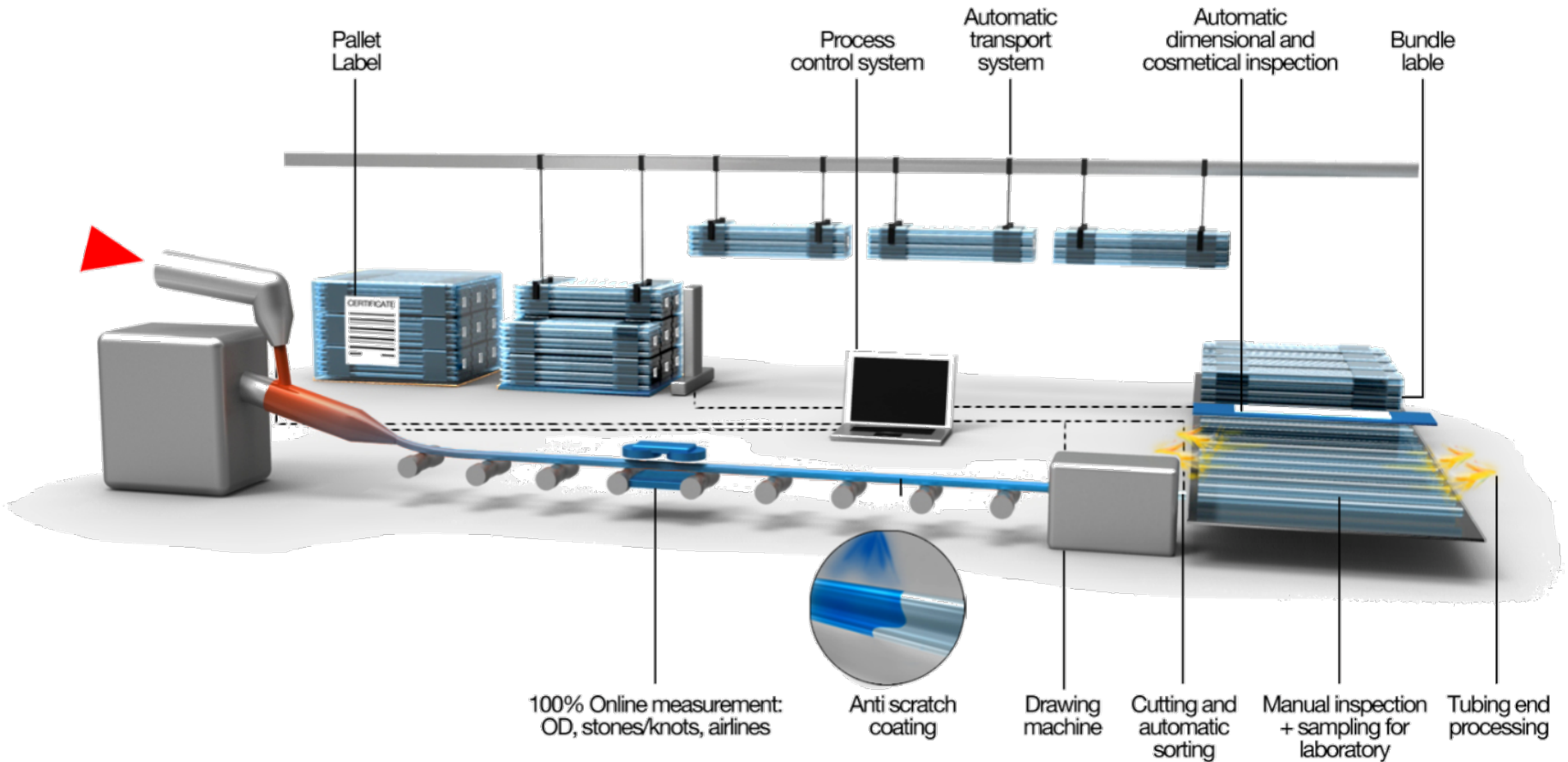
**Melting tank**



**Danner Mandrel**

Graphic is courtesy of SCHOTT Pharmaceutical Systems

# Tubing Manufacturing Process



Graphic is courtesy of SCHOTT Pharmaceutical Systems

# Key Player Glass Syringes



**GERRESHEIMER**



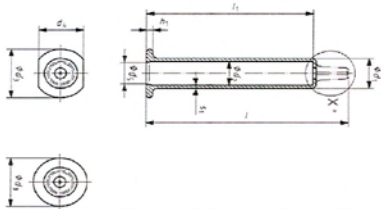
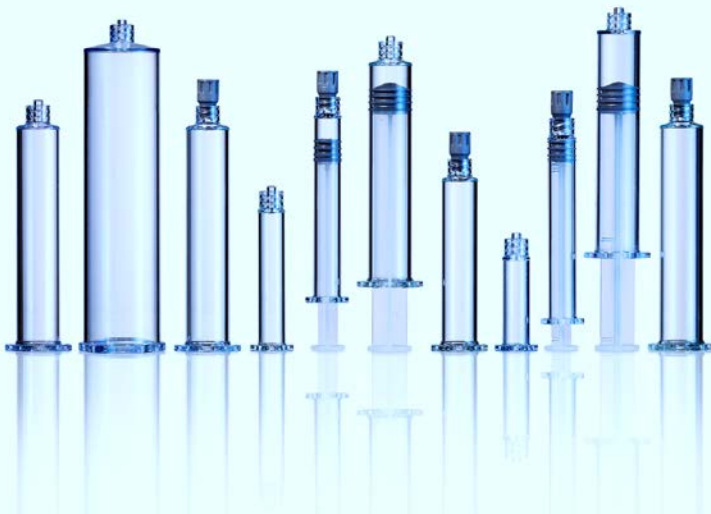
Non limitative list

Logos taken from companies webpages

# Materials for Syringe Systems

Polymer Formats up to 100ml

## POLYMER



Syringe Size	OD [mm]	OD ± [mm]	ID [mm]	ID ± [mm]
0.5 ml	6.8 – 8.2 6-8 – 9.4*	0.10	4.6 – 4,8	0.10
1ml lg	8.1 – 9.4	0.10	6.3 – 6,5	0.10
1 – 3 ml	10.8 - 11.4	0.10	8.5 – 8,75	0.10
5 ml	14.4 - 15.0	0.10	11.7 –12.2	0.10
10 ml	16.6 - 18.0	0.10	14.1 –14.7	0.10
20 ml	21.2 - 22.7	0.15	18,9 –19.1	0.15
50 ml	29.2 – 32.3	0.2	26.4 – 29.3	0.2
100 ml	35.2 – 35.5	0.2	31.8 – 32.2	0.2

ISO 11040-6 specified Outer & Inner Diameter Dimensions in Ranges

# Materials for Syringe Systems: Polyolefines

## Cyclic Olefin Copolymer (COC) and Cyclic Olefin Polymer (COP)

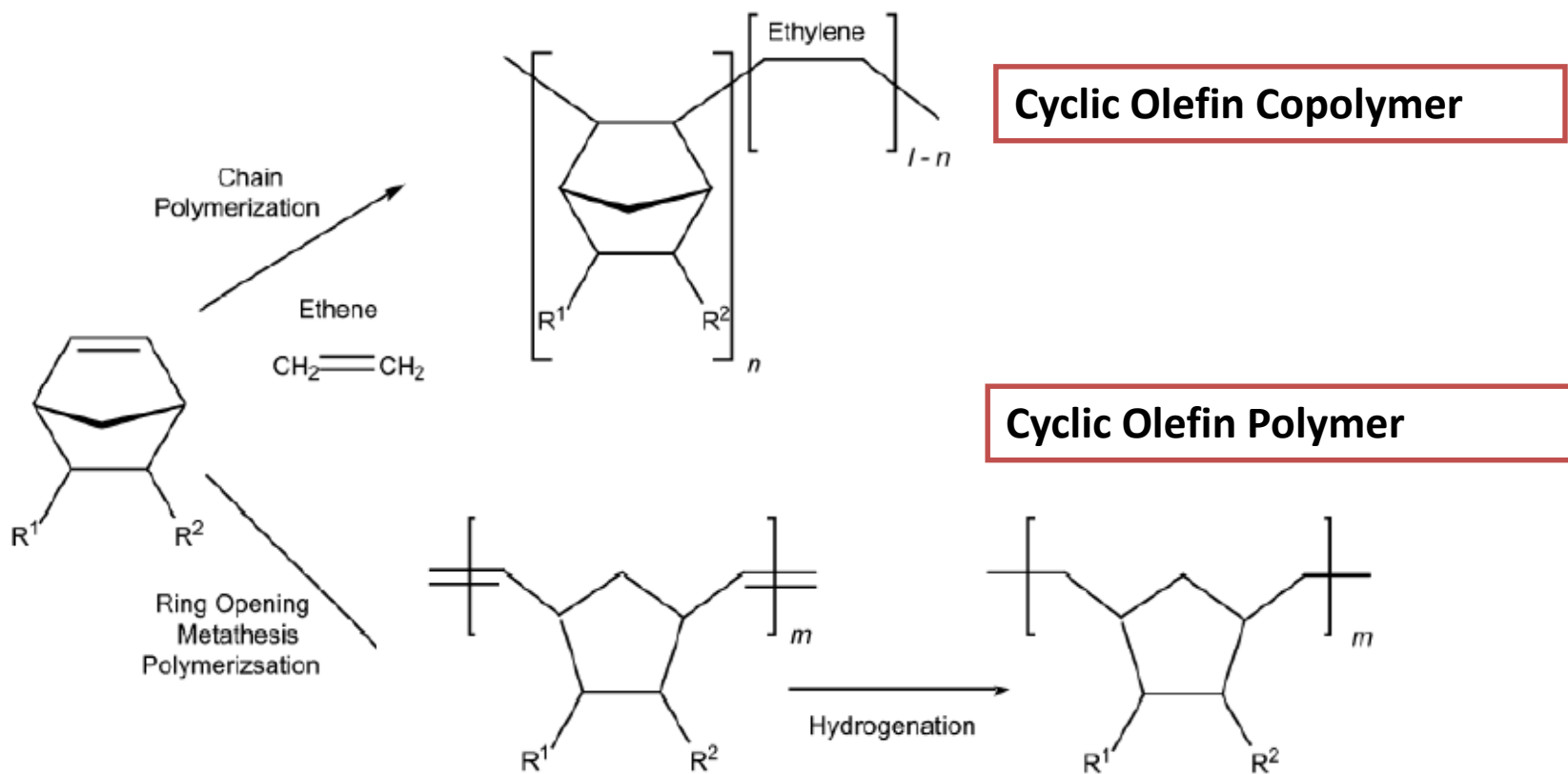
- Amorphous polymer
- Relatively new class of polymers
- Wide variety of applications in films, lenses, medical devices
- No commodities (price)



Logos taken from companies webpages  
Pic is courtesy of SCHOTT Pharmaceutical Systems

# Materials for Syringe Systems: Polyolefines

## Cyclo Olefine Copolymer (COC) and Cyclo Olefine Polymer (COP) are closely related

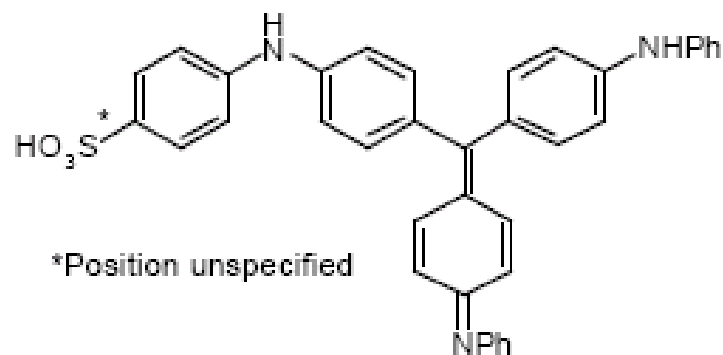
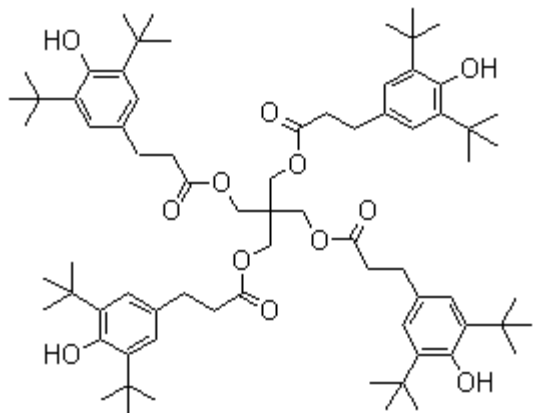


Non limitative list

# Materials for Syringe Systems: Polyolefines

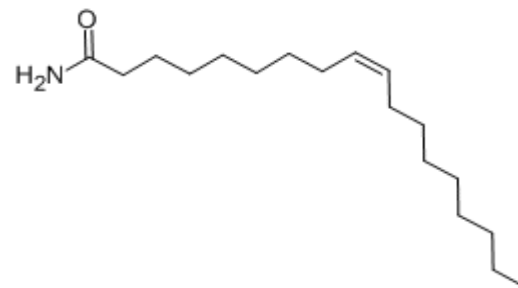
**Stabilizer** : Irganox 1010

Pentaerythritol Tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate)



**Colorant**: Ultramarine Blue

**Slip additives**: Oleamide, Erucamide





# Materials for Syringe Systems: Polyolefines



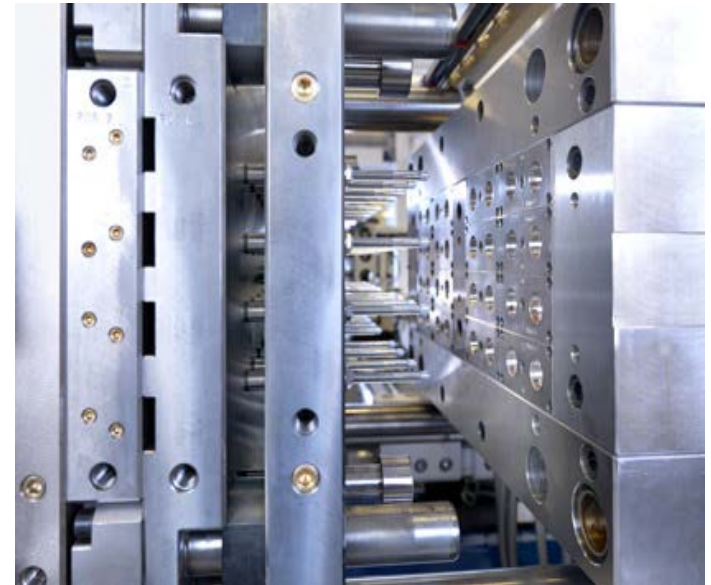
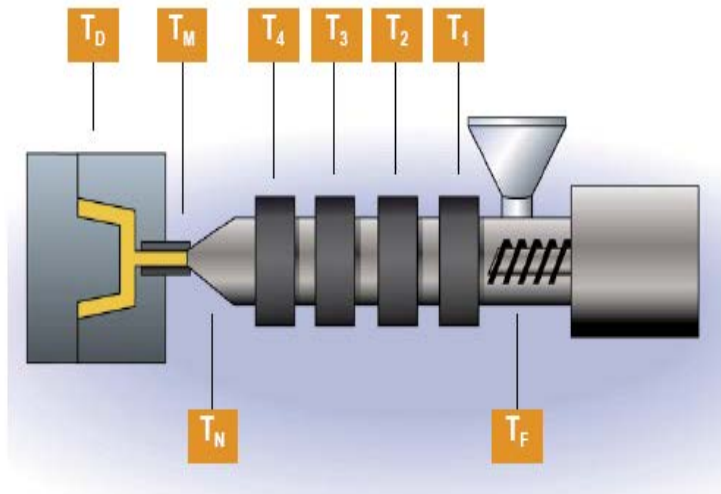
# ZEON

Company	Name	Type
Japan Synthetic Rubber	Arton™	COC
Mitsui Chemicals	APEL™	COC
Topas Advanced Polymers	Topas®	COC
Zeon Corp	Zeonex	COP

Non limitative list

Logos taken from companies webpages

# Manufacturing Process: Injection Molding



Processing temperature  $T_F = < 100 \text{ }^\circ\text{C}$   
 $T_1 = 230 - 260 \text{ }^\circ\text{C}$   
 $T_2 = 240 - 270 \text{ }^\circ\text{C}$   
 $T_3 = 250 - 280 \text{ }^\circ\text{C}$   
 $T_4 = 260 - 290 \text{ }^\circ\text{C}$   
 $T_N = 240 - 300 \text{ }^\circ\text{C}$   
 $T_M = 240 - 300 \text{ }^\circ\text{C}$

Mold-temperature:  $T_D = 95 - 130 \text{ }^\circ\text{C}$

Max. residence time  $< 15 \text{ min}$ ; short interruption to cycle: reduce  $T_x = 170 \text{ }^\circ\text{C}$  !

Injection pressure:  $P_{Sp} = 500 - 1100 \text{ bar (specific)}$

Hold on pressure:  $P_N = 300 - 600 \text{ bar (specific)}$

Back pressure:  $P_{St} = 150 \text{ bar max. (specific)}$

Screw speed:  $n_s = 50 - 200 \text{ rpm}$

Injection speed: moderate to fast (50 mm/sec - 150 mm/sec)

Nozzle type: free - flow

- Note:
- Shrinkage is dependent on processing conditions and part design. Typical shrinkage values are 0,4 - 0,7%
  - Topas Advanced Polymers recommends only external heated hot runner systems.
  - For molded parts with especially high requirements to the surface quality we recommend to choose the highest possible mold temperature.

# Key Players Polymer Syringes

## Prefillable Polymer Syringe Offerings

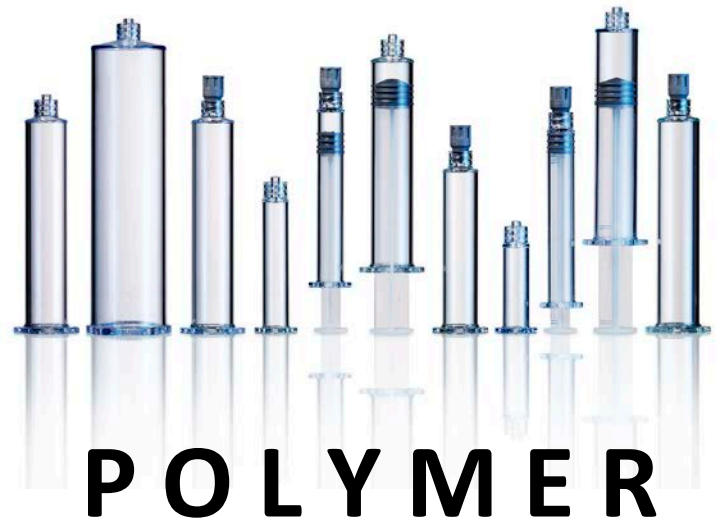
Company	Resin	Brand
Becton Dickinson	COP	BD Sterifill™ SCF™
Gerresheimer Taisei Kako	COP	ClearJect™
Schott Schweiz	COC	SCHOTT TopPac®
SiO <sub>2</sub> Medical Products	COP	Barrier Coated Systems
Terumo	COP	Playjex™
West (Daikyo)	COP	CZ® RU system

# What Material is the BETTER Choice ?

## GLASS



**vs.**



## POLYMER

# Advantages and Disadvantages of Materials

Polymer Vs. Glass



Vs.



Feature	Polymer	Glass
Absence of Heavy Metal's	👍	
Breakage Resistance	👍	
Design Space / customizing	👍	
Discoloration by radiation		👍
Haze Formation		👍

# Advantages and Disadvantages of Materials

Polymer Vs. Glass



Vs.



Feature	Polymer	Glass
Integrated Luer Lock	👍	
Low E & L Profile	👍	
„long term“ experience		👍
Multiple Supply Source		👍
Permeability (gases)	👍	👍

# Advantages and Disadvantages of Materials

Polymer Vs. Glass



Vs.



Feature	Polymer	Glass
Sterilization Possibilities	👍	
Siliconization (free silicone)	👍	
Temperature Resistance		👍
Tolerances	👍	
Tungsten Free	👍	

# Sterilization Methods

Method	COC/COP	Glass
Autoclave 121° C, 20 min <sup>1)</sup>	yes	yes
Gamma irradiation, 25 kGy <sup>2)</sup>	yes	<u>no</u>
Electron radiation <sup>2)</sup>	yes	<u>no</u>
X-Ray <sup>2)</sup>	yes	<u>no</u>
Heat tunnel 280° C, 5 min	<u>no</u>	yes
Ethylene oxide	yes	yes

1) Minimal change in transparency and color, maintains mechanical properties

2) Maintains mechanical properties, no influence on transparency, some color change



# Rubber Components for PFS

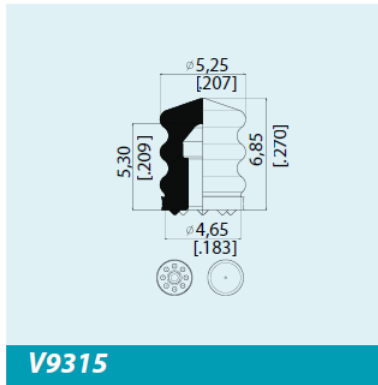
## Major Suppliers for PFS Rubber Components

1. **Aptar Stelmi:** <http://www.aptar.com/pharma/injectables/>
2. **Datwyler:** <http://sealing.datwyler.com/de/industry-solutions/health-care.html>
3. **West:** <http://www.westpharma.com/en/Pages/Default.aspx>

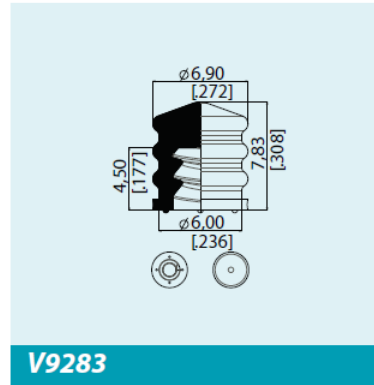
# Rubber Components for PFS

## TYPICAL PRODUCTS

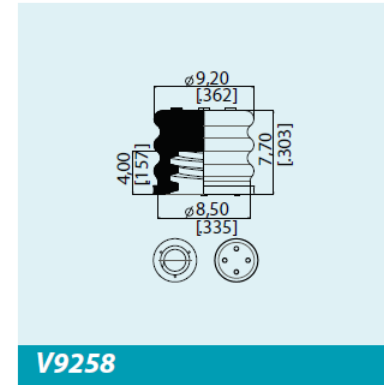
0.5 ml



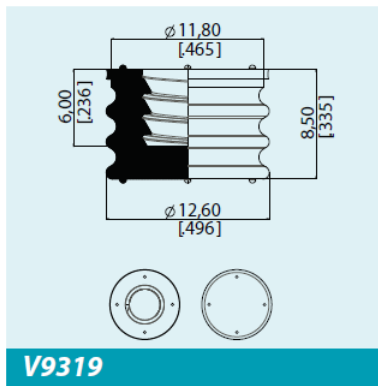
1 ml long



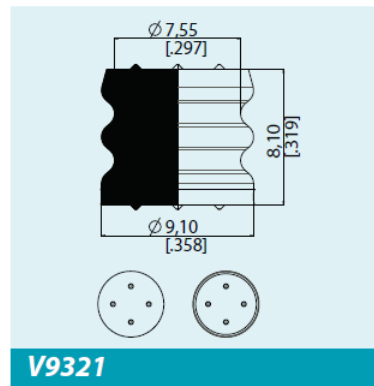
1 - 3 ml



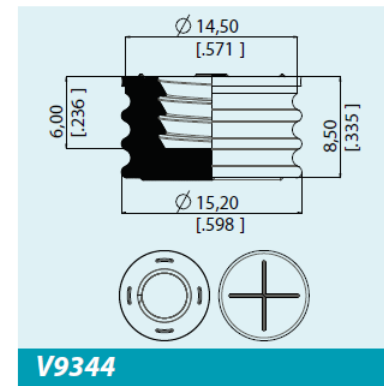
5 ml



Dual chamber plunger



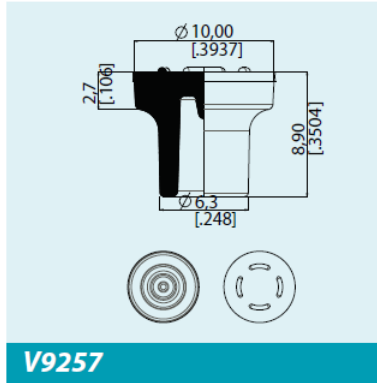
10 ml



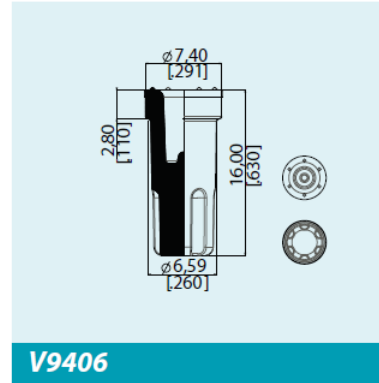
Drawings taken from Datwylers product brochures

# Rubber Components for PFS

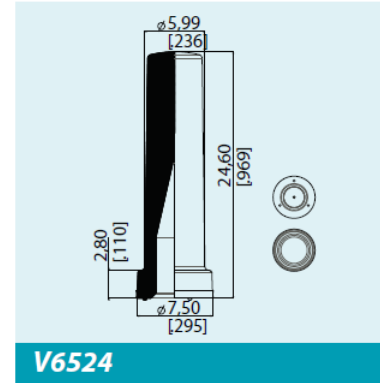
Mushroom Tip Cap



Ribbed Tip Cap



1/2" Needle Shield



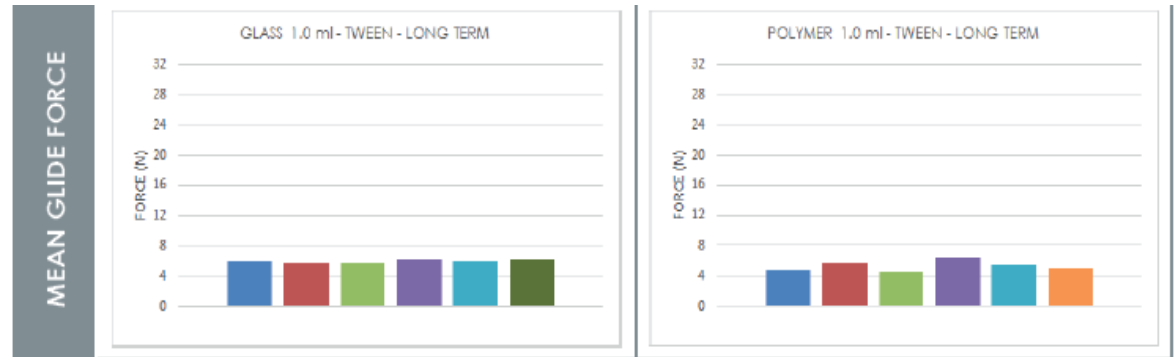
Drawings taken from Datwylers product brochures

Pic is courtesy of SCHOTT Pharmaceutical Systems

# Alternative to Standard Rubber



	CHARACTERISTICS
MATERIAL	THERMOPLASTIC ELASTOMER - EVOPRENE G970
BIOCOMPATIBILITY	ISO 11040-5, ISO 10993-5, 1999, USP 27, NF 22, 2004 - CLASS VI70°C
STERILIZATION	GAMMA IRRADIATION, STEAM (relaxed), NONE - by customer choice
BREAK LOOSE & GLIDE FORCES	ISO 11040-8 Annex E
CONTAINER CLOSURE	ASTM F1929
PERMEABILITY	ICH Q1A(R2)
EXTRACTABLES	DS/EN ISO 8871-1:2005



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Thank You !  
QUESTIONS ?