



Test Methods for Prefilled Syringes

19&20 October 2023, Gothenburg, Sweden

Horst Koller, CEO, HK Packaging Consulting GmbH

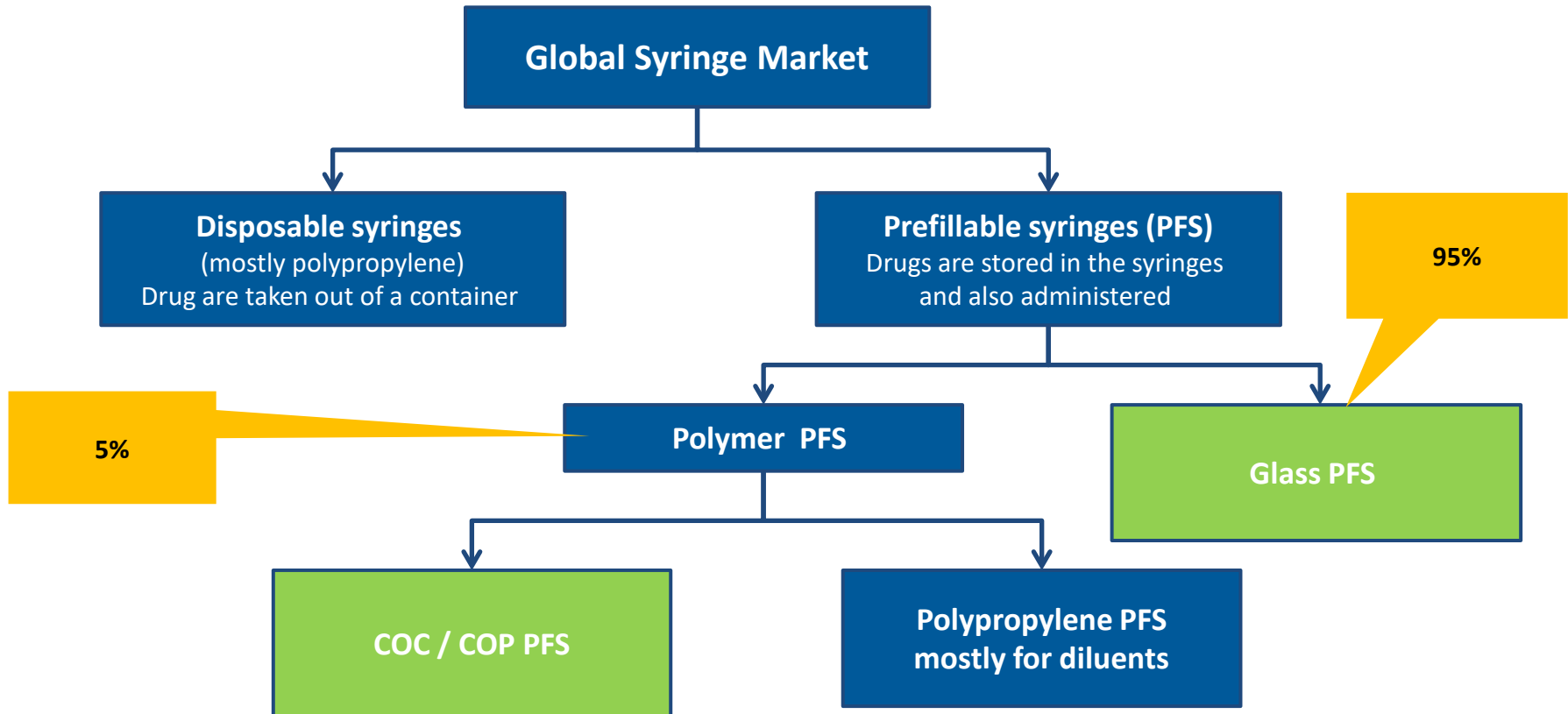
Erik Berndt, Industry Manager – Medical and Pharmaceutical, ZwickRoell GmbH & Co. KG

- **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

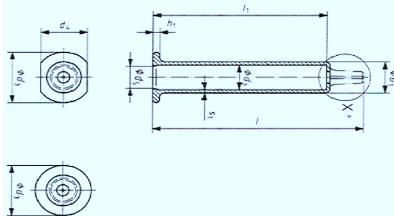
Pre-Sterilized syringes are delivered in tub and nest and are ready for filling at customers.



Materials for Syringe Systems

Glass Formats up to 20ml,

GLASS



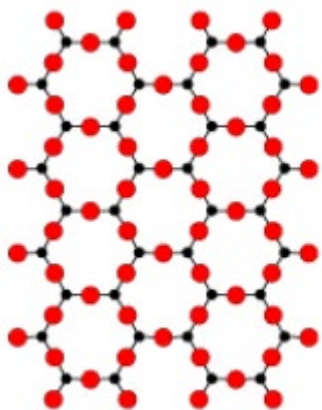
Syringe Size	OD [mm]	OD ± [mm]	ID [mm]	ID ± [mm]
0.5 ml	6.85	0.10	4.65	0.10
1 ml lg	8.15	0.10	6.35	0.10
1 – 3 ml	10.85	0.10	8.65	0.20
5 ml	14.45	0.10	11.85	0.20
10 ml	17.05	0.20	14.25	0.20
20 ml	22.05	0.20	19.05	0.20

ISO 11040-4 specified Outer & Inner Diameter Dimensions



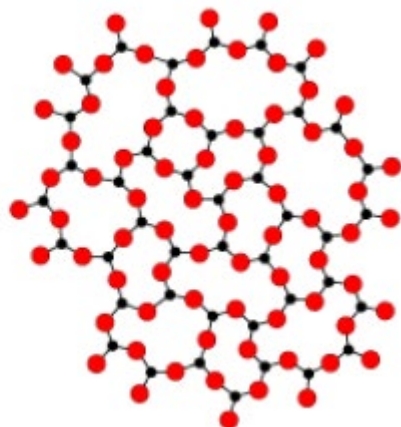
Outer Diameter: 1ml std $9,2 \pm 0.1\text{mm}$

Materials for Syringe Systems: Glass



Quartz crystal

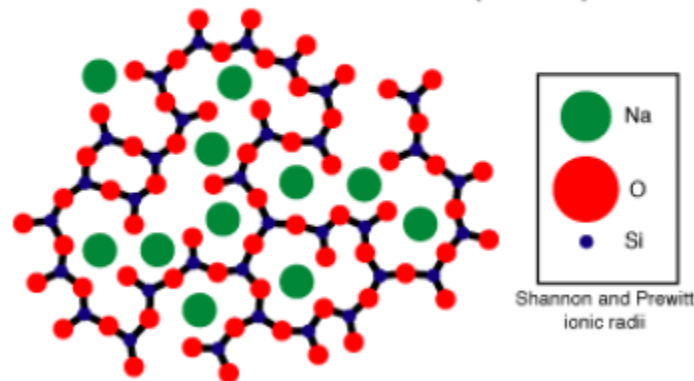
MP >2000° C



Quartz glass

MP ~1700° C

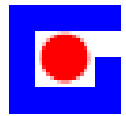
Proposed Structure of Sodium Silicate Glass
after Warren and Biscoe (1930's)



- ❑ 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 : SiO_2 (SiO_4^{4-})
 - ❑ Network modifiers to lower melting point - Na_2O , B_2O_3 , PbO
 - ❑ Stabilizers to improve durability - CaO , Al_2O_3
 - ❑ Colorants as needed - Fe_2O_3 - TiO_2 & many others

Materials for Syringe Systems: Glass

CORNING



Nippon Electric Glass Co., Ltd.



NIPRO

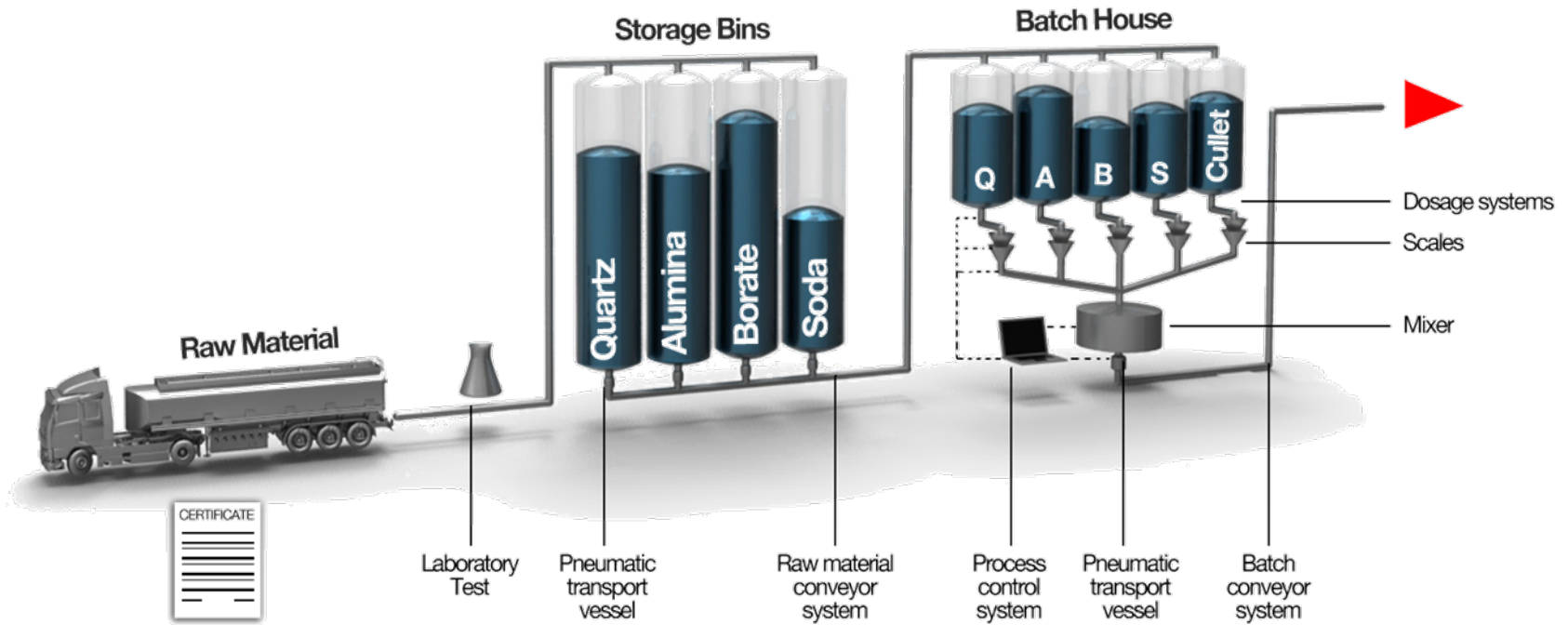


SCHOTT
glass made of ideas

Non limitative list

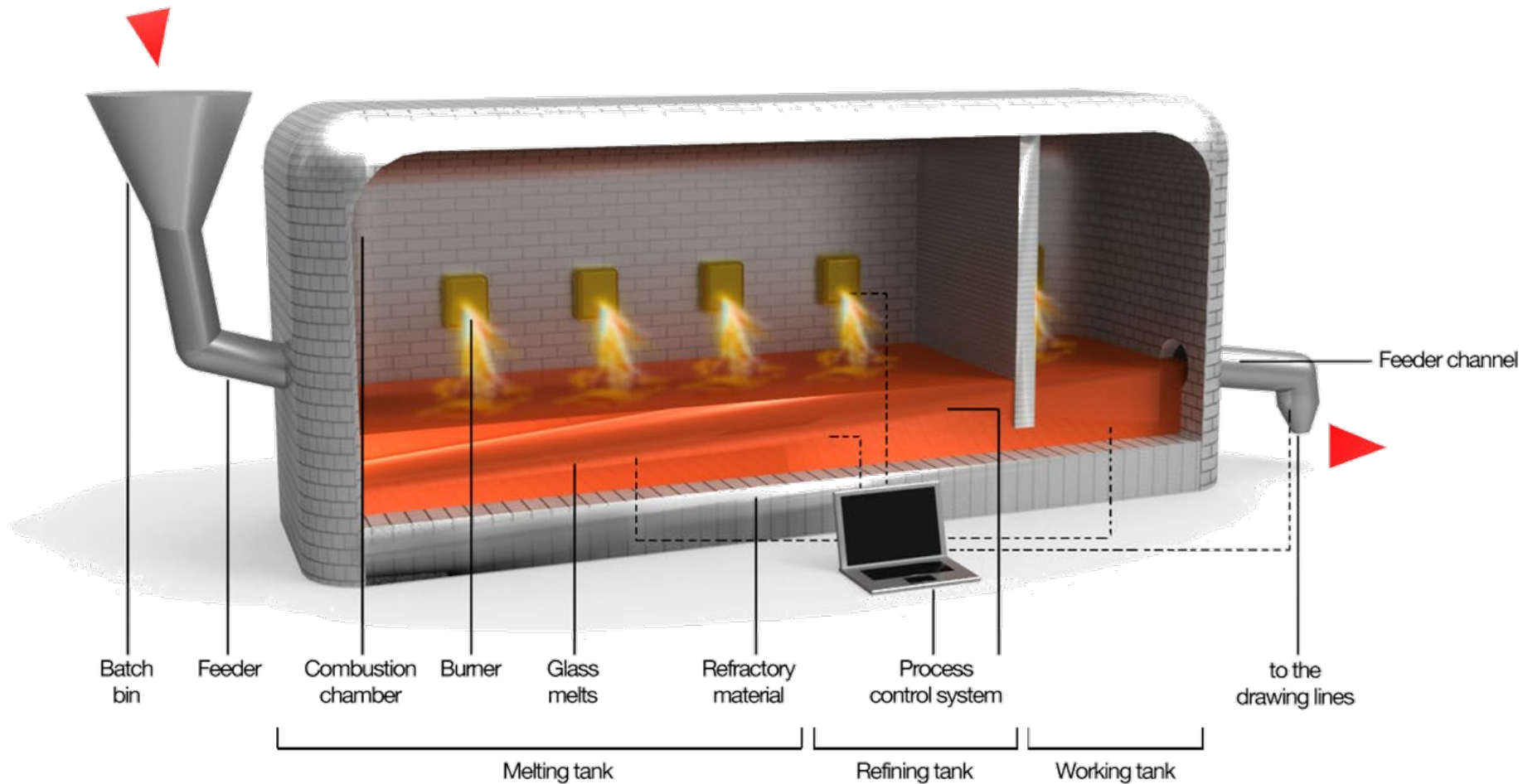
Logos taken from companies webpages

Tubing Manufacturing Process



Graphic is courtesy of SCHOTT Pharmaceutical Systems

Tubing Manufacturing Process



Graphic is courtesy of SCHOTT Pharmaceutical Systems

Tubing Manufacturing Process



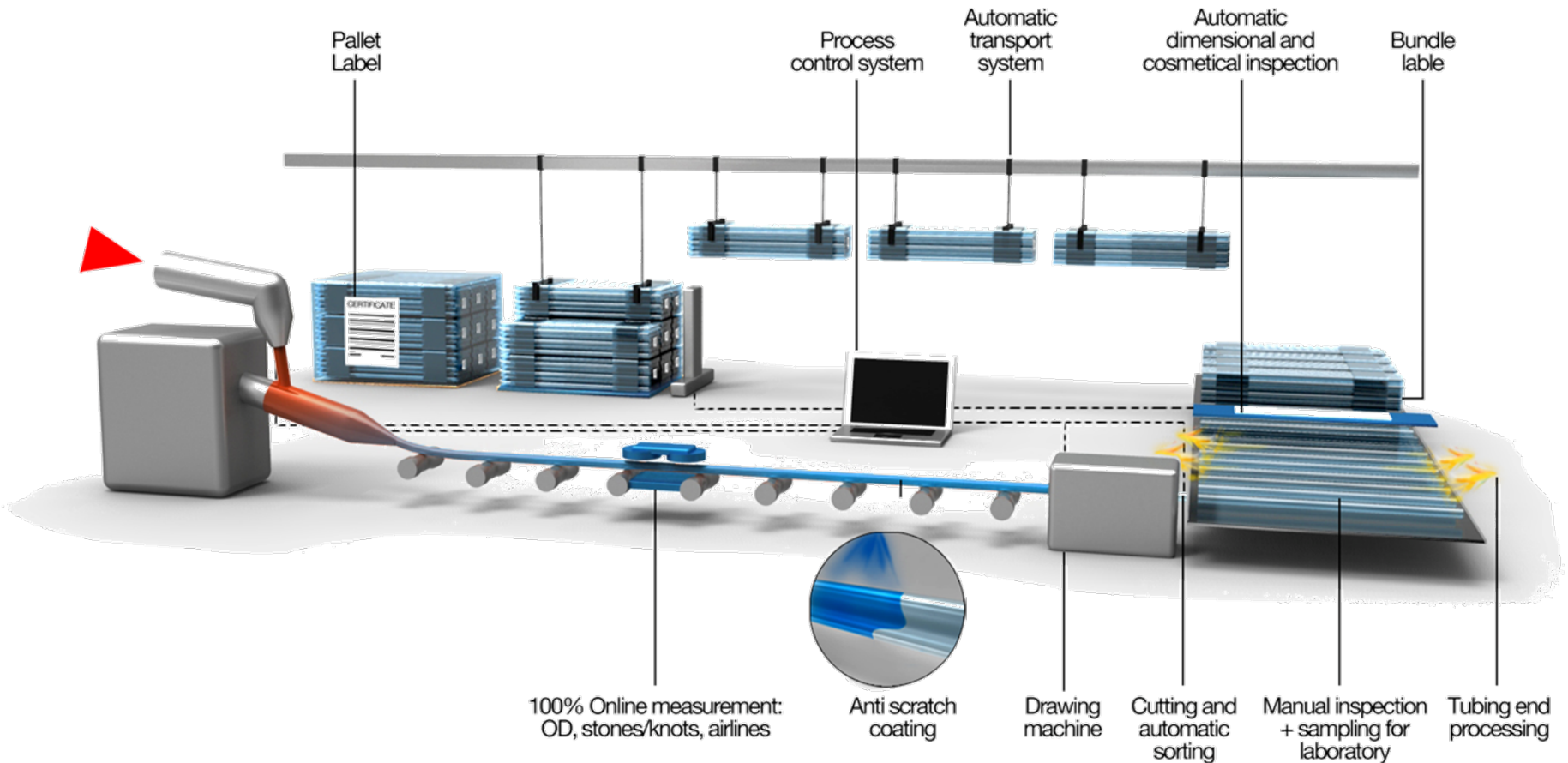
Melting tank



Danner Mandrel

Graphic is courtesy of SCHOTT Pharmaceutical Systems

Tubing Manufacturing Process



Graphic is courtesy of SCHOTT Pharmaceutical Systems

Key Player Glass Syringes



GERRESHEIMER



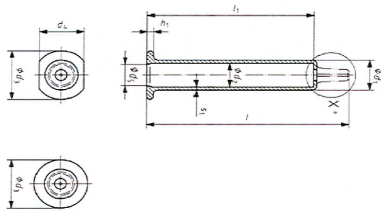
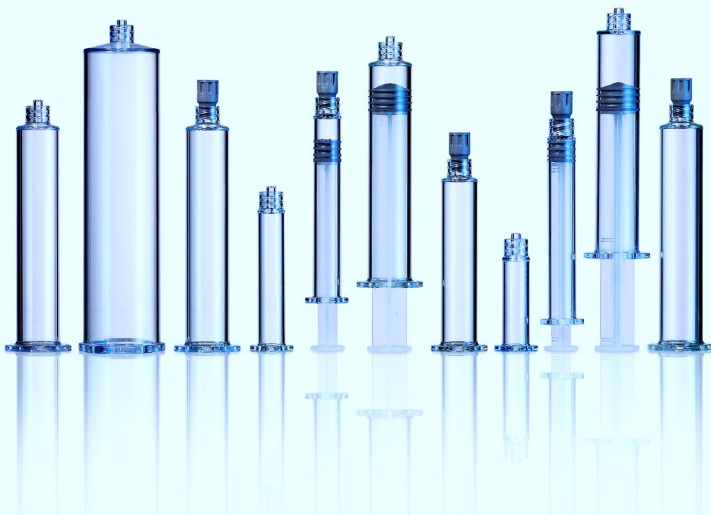
Non limitative list

Logos taken from companies webpages

Materials for Syringe Systems

Polymer Formats up to 100ml

POLYMER

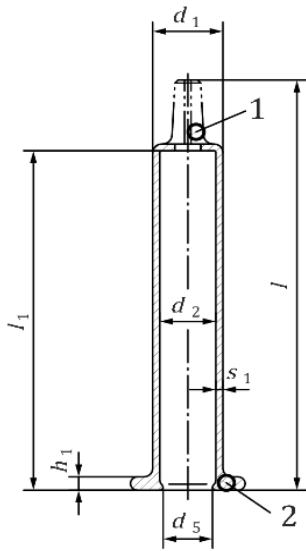


Syringe Size	OD [mm]	OD ± [mm]	ID [mm]	ID ± [mm]
0.5 ml	6.8 – 8.2 6-8 – 9.4*	0.10	4.6 – 4,8	0.10
1ml lg	8.1 – 9.4	0.10	6.3 – 6,5	0.10
1 – 3 ml	10.8 - 11.4	0.10	8.5 – 8,75	0.10
5 ml	14.4 - 15.0	0.10	11.7 –12.2	0.10
10 ml	16.6 - 18.0	0.10	14.1 –14.7	0.10
20 ml	21.2 - 22.7	0.15	18,9 –19.1	0.15
50 ml	29.2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

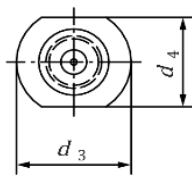
Materials for Syringe Systems

Dimensions in millimetres

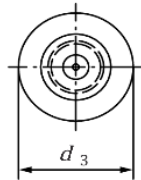


Nominal volume ml	Nominal dimension tolerances						
	d_1	d_2^a	l	l_1	h_1	d_3	d_4
0,5	6,8 to 8,2 ± 0,1 6,8 to 9,7 ± 0,1 ^b	4,6 to 4,8 ± 0,1	57,0 to 64,8 ± 0,2	47,5 to 54,1 ± 0,2	1,8 to 2,1 ± 0,1	13,4 to 13,8 ± 0,1	10,5 to 11,0 ± 0,1
1 ^c	8,1 to 9,7 ± 0,1	6,3 to 6,5 ± 0,1	64,0 to 64,5 ± 0,2	54,0 to 54,5 ± 0,2	1,9 to 2,3 ± 0,1	13,7 to 13,8 ± 0,1	10,5 to 11,0 ± 0,1
1 ^d	10,8 to 11,4 ± 0,1	8,5 to 8,75 ± 0,1	45,9 to 46,9 ± 0,2	35,2 to 35,9 ± 0,2	1,9 to 2,3 ± 0,1	17,75 ± 0,1	14,70 ± 0,1
2,25	10,8 to 11,4 ± 0,1	8,5 to 8,75 ± 0,1	64,4 to 66,8 ± 0,2	53,9 to 54,6 ± 0,2	1,9 to 2,3 ± 0,1	17,75 ± 0,1	14,70 ± 0,1
3	10,8 to 11,6 ± 0,1	8,5 to 8,75 ± 0,1	82,4 to 84,6 ± 0,2	71,7 to 72,4 ± 0,2	1,9 to 2,3 ± 0,1	17,75 ± 0,1	14,70 ± 0,1
5	14,4 to 15,0 ± 0,1	11,7 to 12,2 ± 0,1	76,5 to 80,0 ± 0,2	64,3 to 66,7 ± 0,2	2,0 to 3,1 ± 0,15	22,9 to 23,1 ± 0,1	19,40 to 19,9 ± 0,1
10	16,6 to 18,0 ± 0,1	14,1 to 14,7 ± 0,1	97,7 to 100,5 ± 0,3	86,2 to 87,3 ± 0,2	2,0 to 3,1 ± 0,15	26,9 to 27,4 ± 0,1	21,50 to 21,9 ± 0,1
20	21,2 to 22,7 ± 0,15	18,2 to 19,1 ± 0,15	107,3 to 120,2 ± 0,3	95,6 to 109,1 ± 0,2	2,0 to 3,1 ± 0,15	32,25 to 39,0 ± 0,15	25,15 to 26,1 ± 0,15
50	29,2 to 32,3 ± 0,2	26,4 to 29,3 ± 0,2	128,8 to 151,2 ^e ± 0,5	118,7 to 128,2 ^e ± 0,5	2,0 to 3,5 ± 0,2	45,00 to 50,1 ± 0,2	33,2 to 39,10 ± 0,2
100	35,2 to 35,5 ± 0,2	31,8 to 32,2 ± 0,2	169,8 ± 0,5	156,4 ± 0,5	2,7 to 3,1 ± 0,2	47,65 ± 0,2	41,45 ± 0,2

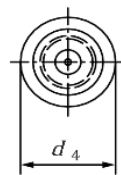
^a For the specification of the inner diameter, the specification of the plunger shall be considered with regard to break loose force and sustaining force as well as for plunger/barrel seal tightness. The size of the inner diameter also depends on the polymer material.
^b This range is dedicated to barrels with an integrated Luer lock.
^c Long.
^d Short or standard.
^e This range is required in order to consider particular applications, such as pumps and injectors.



a) cut-flange



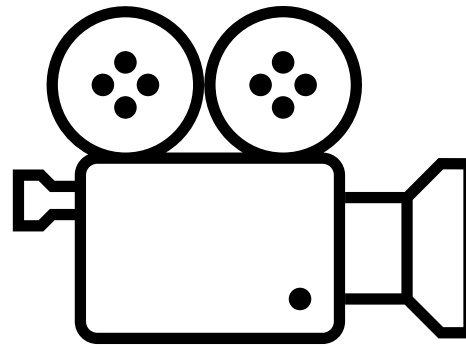
b) round flange



c) small-round flange

Extract from ISO 11040-6 Plastic barrel dimensions

From Tubing To Syringe



Materials for Syringe Systems: Polyolefines

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

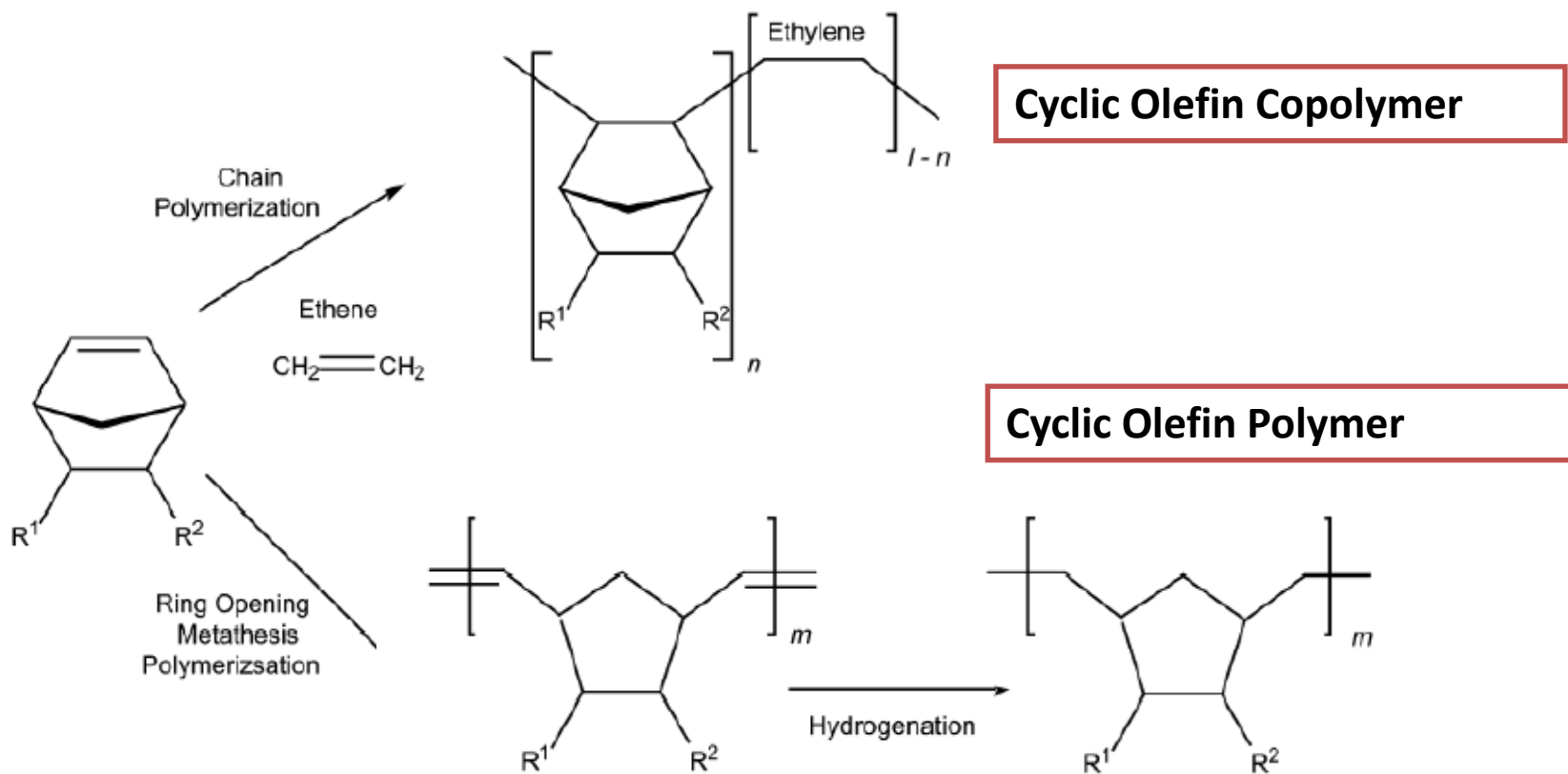
- Amorphous polymer
- Relatively new class of polymers
- Wide variety of applications in films, lenses, medical devices
- No commodities (price)



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

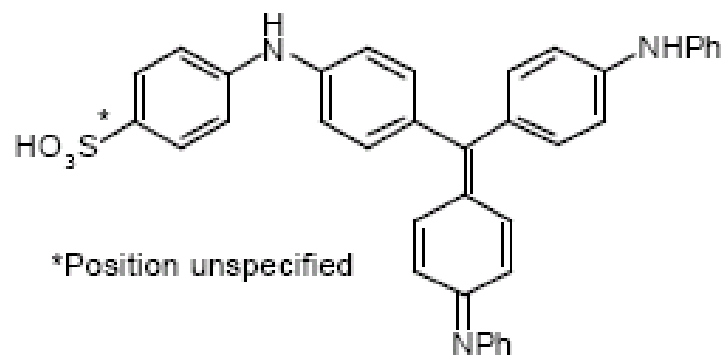
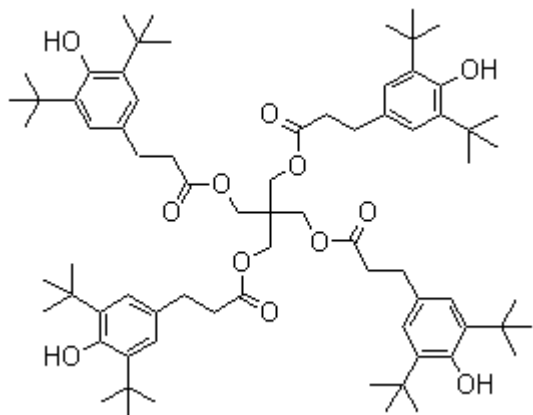


Non limitative list

Materials for Syringe Systems: Polyolefines

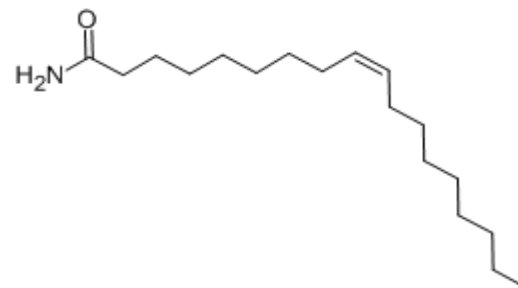
Stabilizer : Irganox 1010

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



Colorant: Ultramarine Blue

Slip additives: Oleamide, Erucamide



Materials for Syringe Systems: Polyolefines

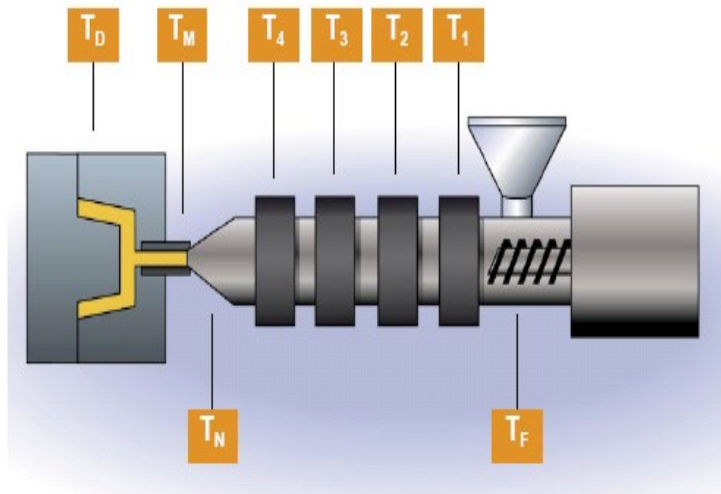


Company	Name	Type
Japan Synthetic Rubber	Arton™	COC
Mitsui Chemicals	APEL™	COC
Topas Advanced Polymers	Topas®	COC
Zeon Corp	Zeonex	COP

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

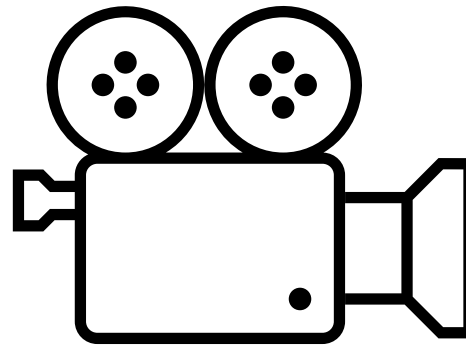
Screw speed: $n_s = 50 - 200 \text{ rpm}$

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.

Manufacturing Process: Injection Molding



Non limitative list

Key Players Polymer Syringes

Prefillable Polymer Syringe Offerings

Company	Resin	Brand
Becton Dickinson	COP	BD Sterifill™ SCF™
Gerresheimer Taisei Kako	COP	ClearJect™
Schott Pharma	COC	SCHOTT TopPac®
SiO ₂ Medical Products	COP	Barrier Coated Systems
Terumo	COP	Plajex™
West (Daikyo)	COP	CZ® RU system
Wirthwein Medical	COC	WIM-Ject™

Key Players Polymer Syringes



GERRESHEIMER

DAIKYO _____
Crystal Zenith®
THE CLEAR SOLUTION

SCHOTT



 **TERUMO**



WIRTHWEIN
MEDICAL

Non limitative list

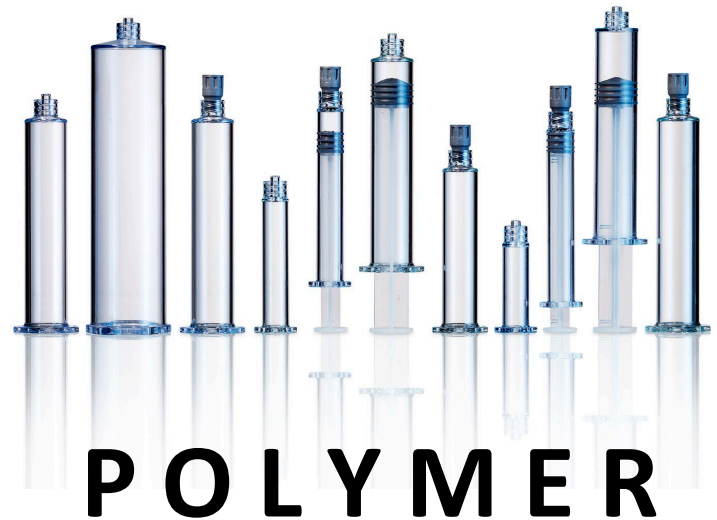
Logos taken from companies webpages

What Material is the BETTER Choice ?

GLASS



vs.



POLYMER

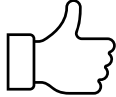
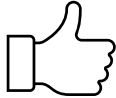
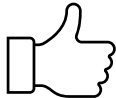

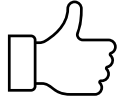
Advantages and Disadvantages of Materials

Polymer	vs.	Glass
---------	-----	-------



vs.



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

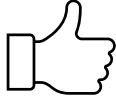
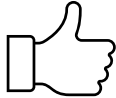
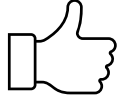


Advantages and Disadvantages of Materials

Polymer	vs.	Glass
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vs.



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

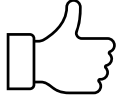

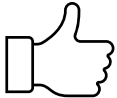
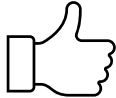

Advantages and Disadvantages of Materials

Polymer	Vs.	Glass
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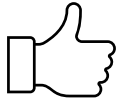



Vs.



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

Sterilization Methods

Sterilization	Polymer	Glass
Autoclaving	possible	
Irradiation (Gamma, X-Ray, E-beam)		
Heat Tunnel		
Gases (VHP, NO2, ETO)	possible	

Rubber Components for PFS

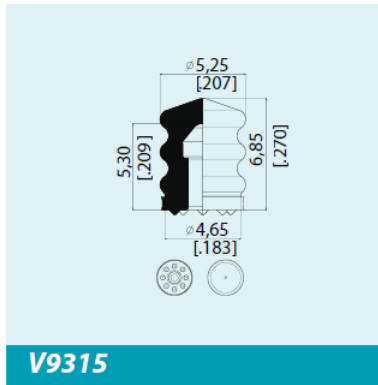
Major Suppliers for PFS Rubber Components

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

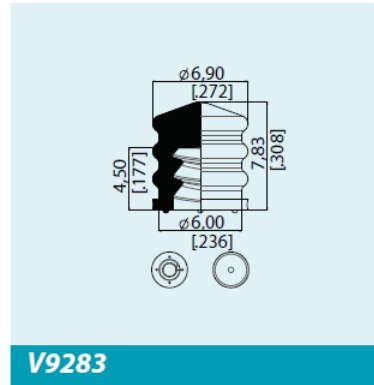
Rubber Components for PFS

TYPICAL PRODUCTS

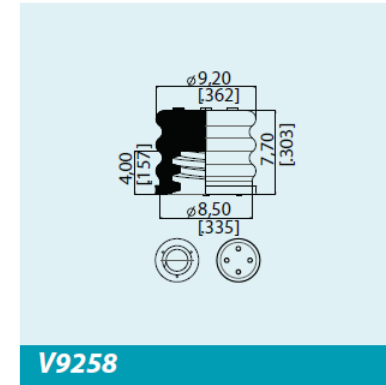
0.5 ml



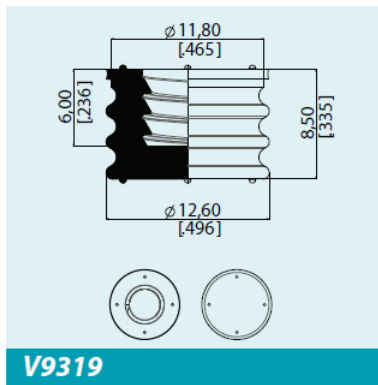
1 ml long



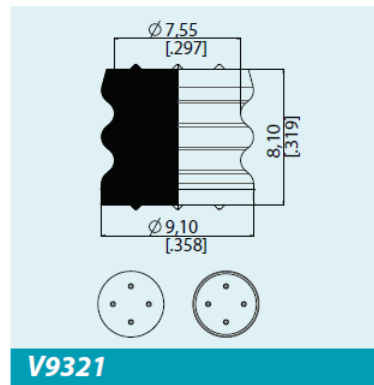
1 - 3 ml



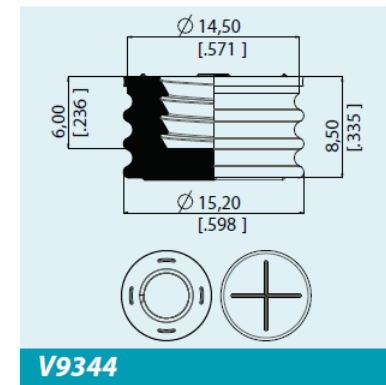
5 ml



Dual chamber plunger



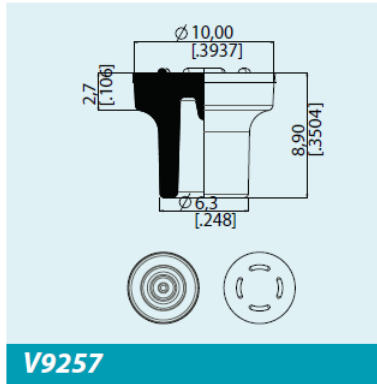
10 ml



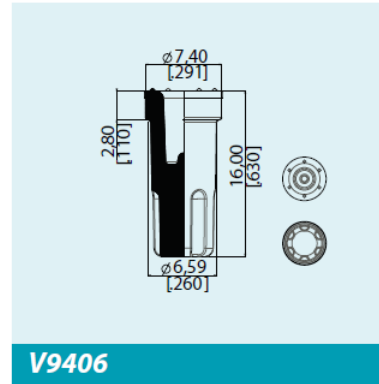
Drawings taken from Datwylers product brochures

Rubber Components for PFS

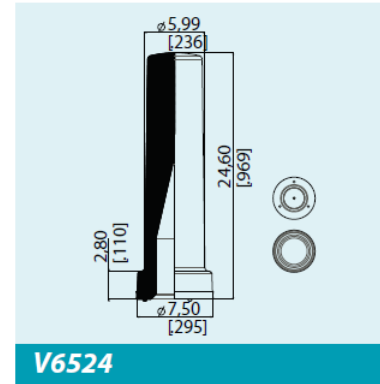
Mushroom Tip Cap



Ribbed Tip Cap



1/2" Needle Shield



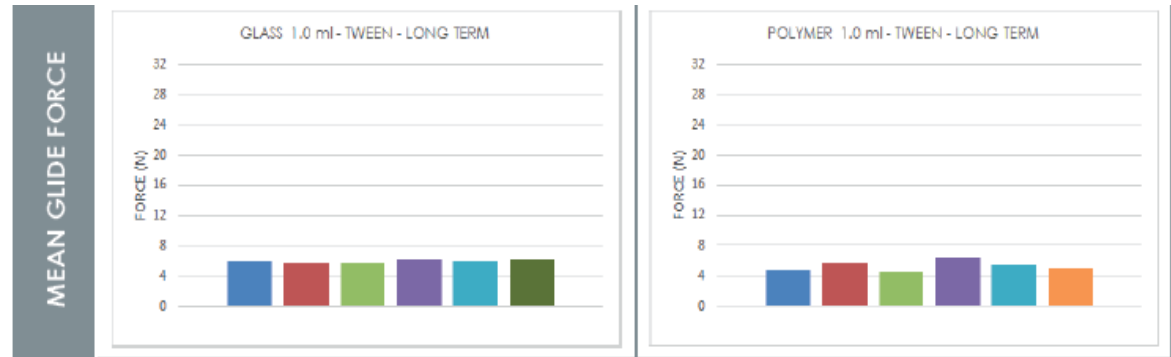
Drawings taken from Datwylers product brochures

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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