Test Methods for Prefilled Syringes

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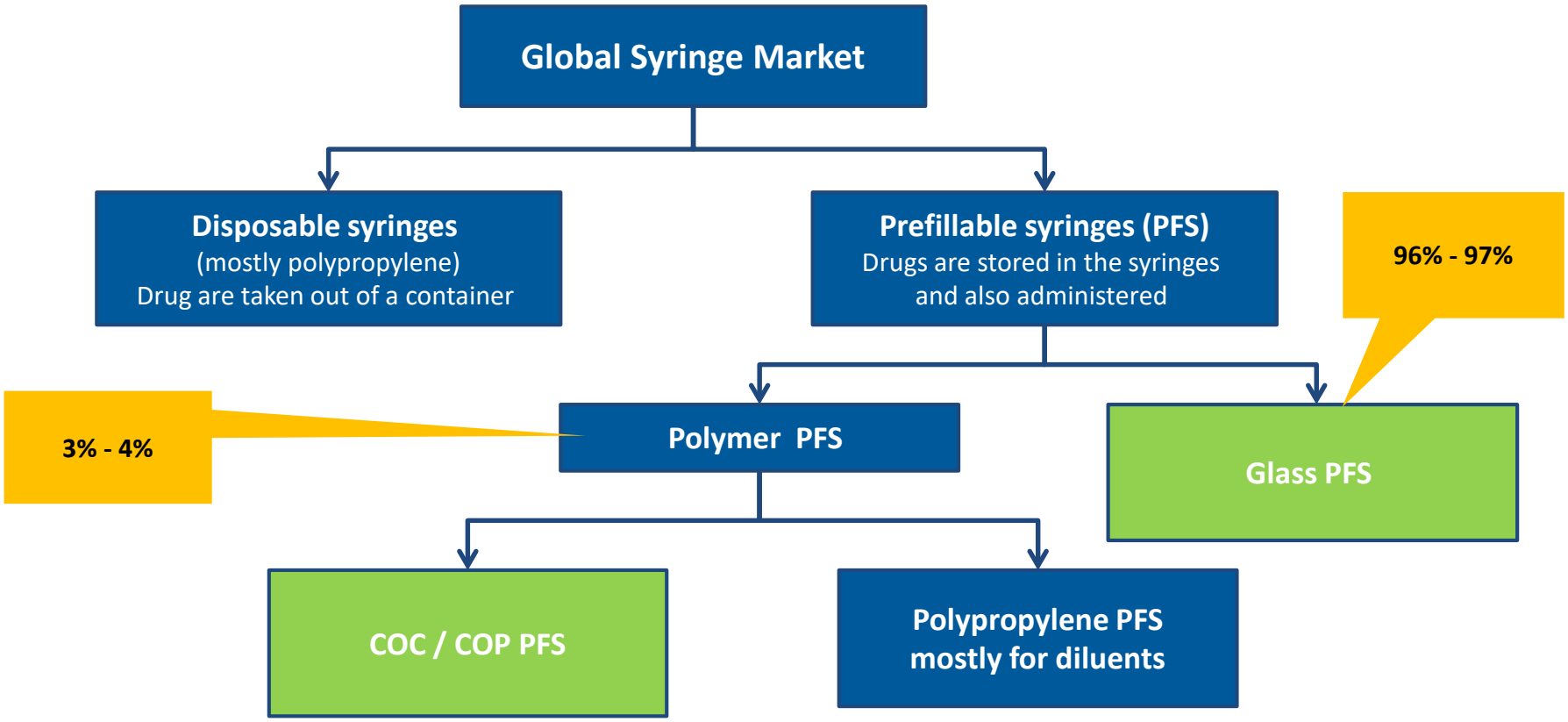
Test Methods for Prefilled Syringes

PART 1:

- **Introduction to Syringe Systems & Components**

Prefilled Syringes

Syringe Market Overview - General



Notes:

COC: Cyclic Olefin Copolymer
COP: Cyclic Olefin Polymer

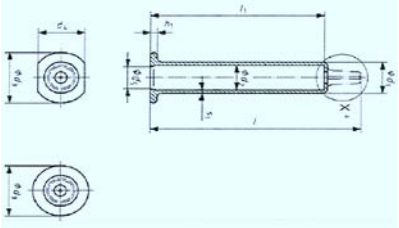
Definition of Prefilled Syringes

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

Bulk Syringes	Prefilled Syringes
Bulk syringes unsterile and were delivered packed in Rondo trays.	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,

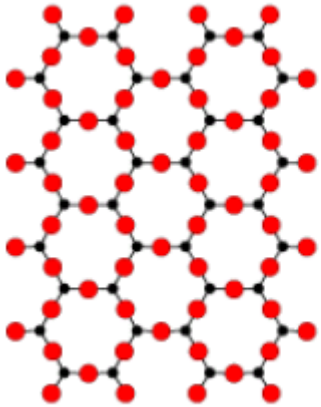


Syringe Size	OD [mm]	OD ± [mm]	ID [mm]	ID ± [mm]
0.5 ml	6.85	0.10	4.65	0.10
1ml lg	8.15	0.10	6.35	0.10
1 – 3 ml	10.85	0.10	8.65	0.20
5 ml	14.45	0.10	11.85	0.20
10 ml	17.05	0.20	14.25	0.20
20 ml	22.05	0.20	19.05	0.20

ISO 11040-4 specified Outer & Inner Diameter Dimensions

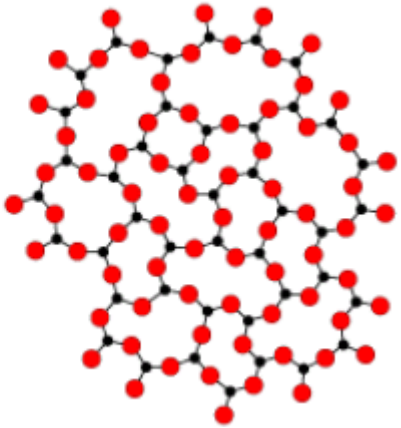
Outer Diameter: 1ml std 9,2 ± 0.1mm

Materials for Syringe Systems: Glass



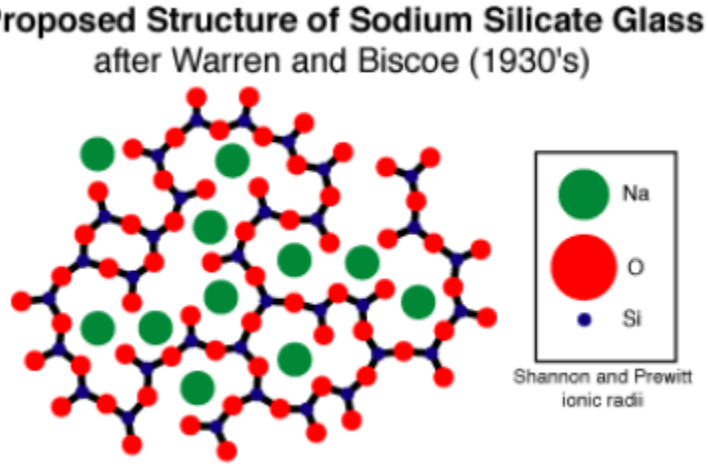
Quarz crystal

MP >2000° C



Quarz glass

MP ~1700° C



- 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 ~500ºC, 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

Pic are courtesy of SCHOTT Pharmaceutical Systems

Materials for Syringe Systems: Glass

CORNING

Nippon Electric Glass Co., Ltd.

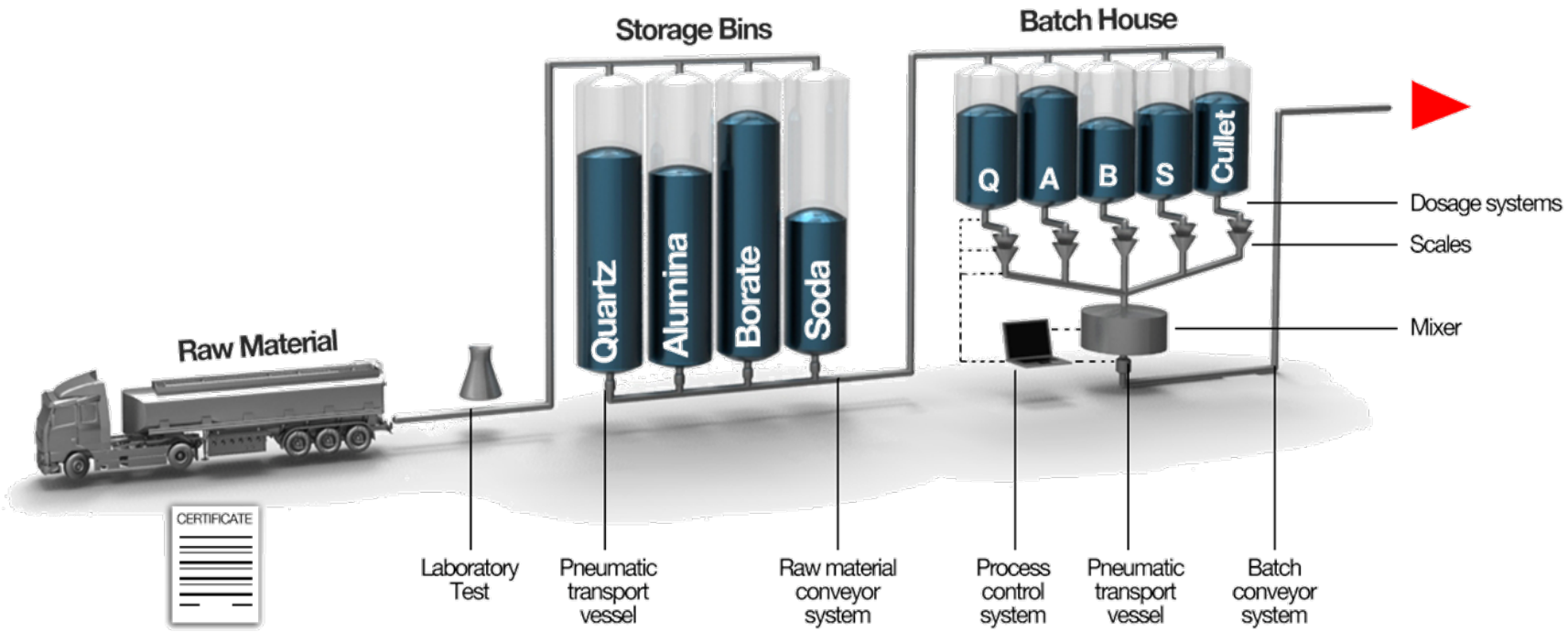
NIPRO

SCHOTT
glass made of ideas

Non limitative list

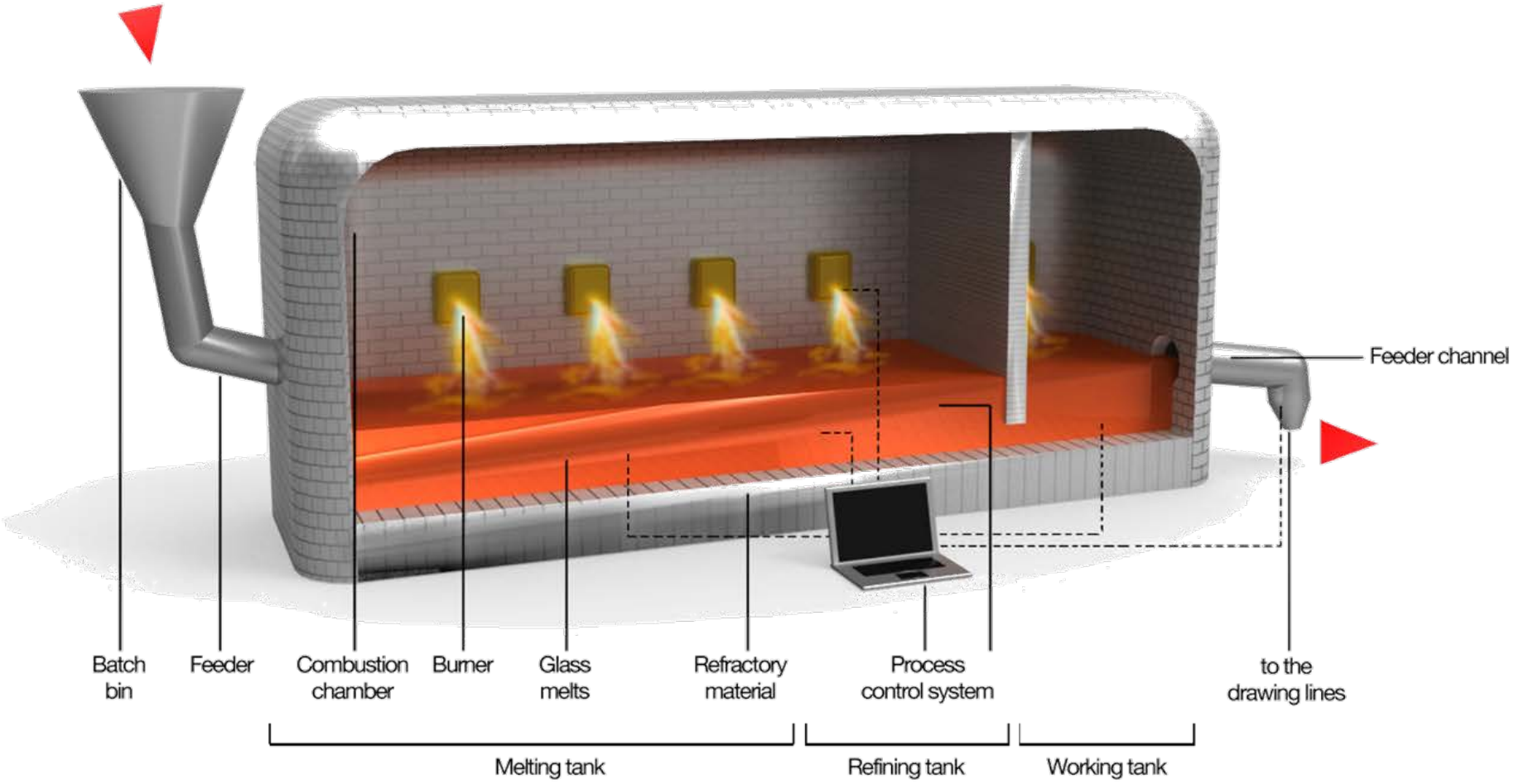
Logos taken from companies webpages

Tubing Manufacturing Process



Graphic is courtesy of SCHOTT Pharmaceutical Systems

Tubing Manufacturing Process



Graphic is courtesy of SCHOTT Pharmaceutical Systems

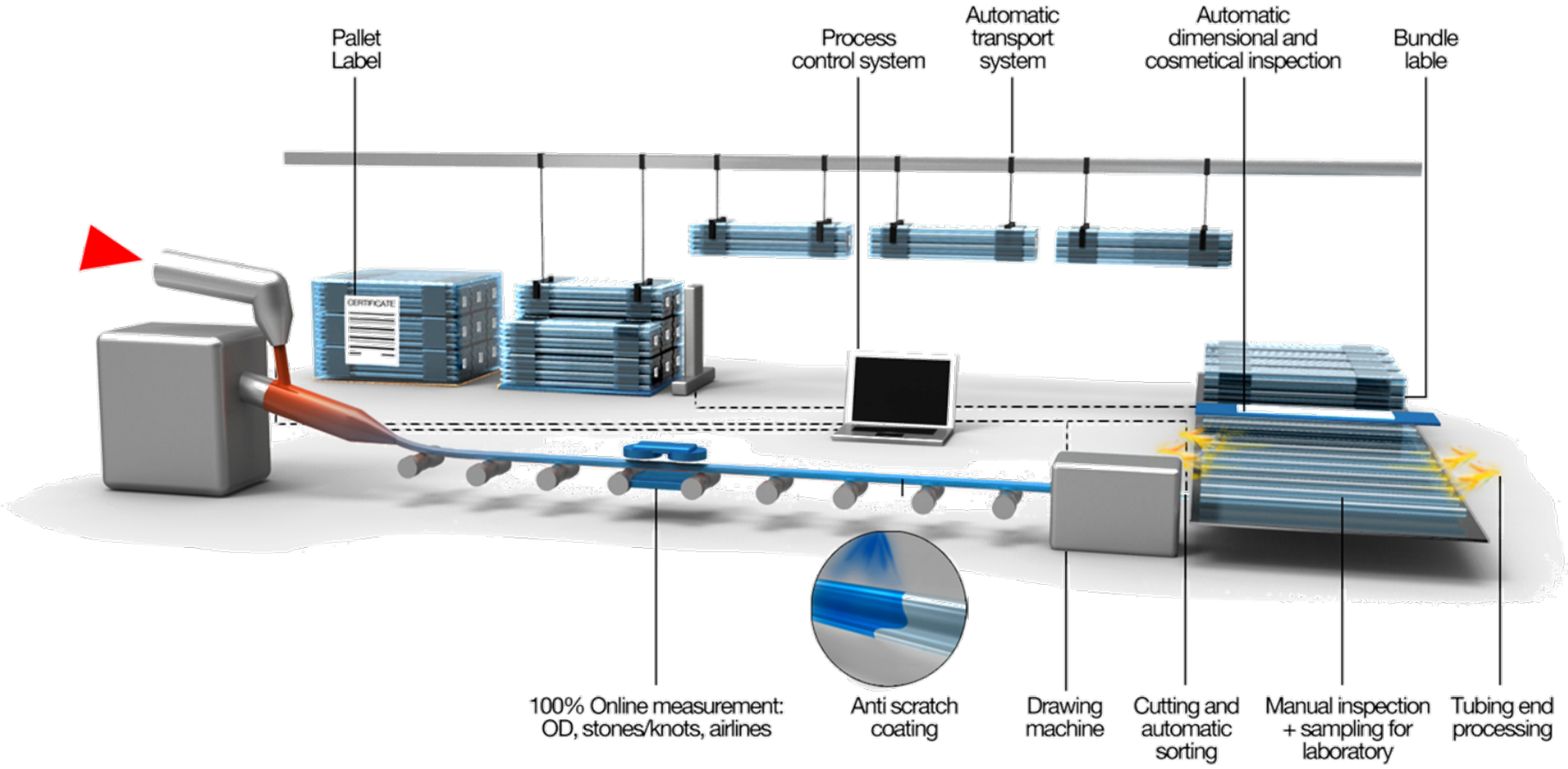
Tubing Manufacturing Process

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

BD
Helping all people live healthy lives

GERRESHEIMER

NIPRO

Nuova Ompi
glass division
Stevanato Group

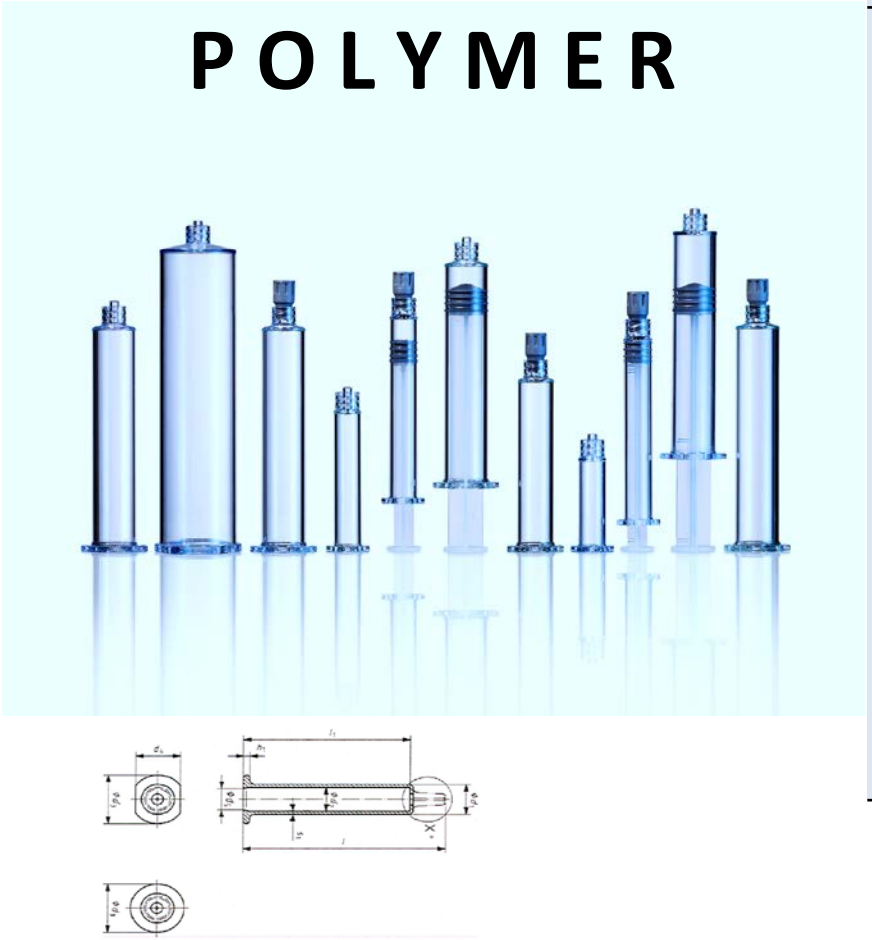
SCHOTT
glass made of ideas

Non limitative list

Logos taken from companies webpages

Materials for Syringe Systems

Polymer Formats up to 100ml



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

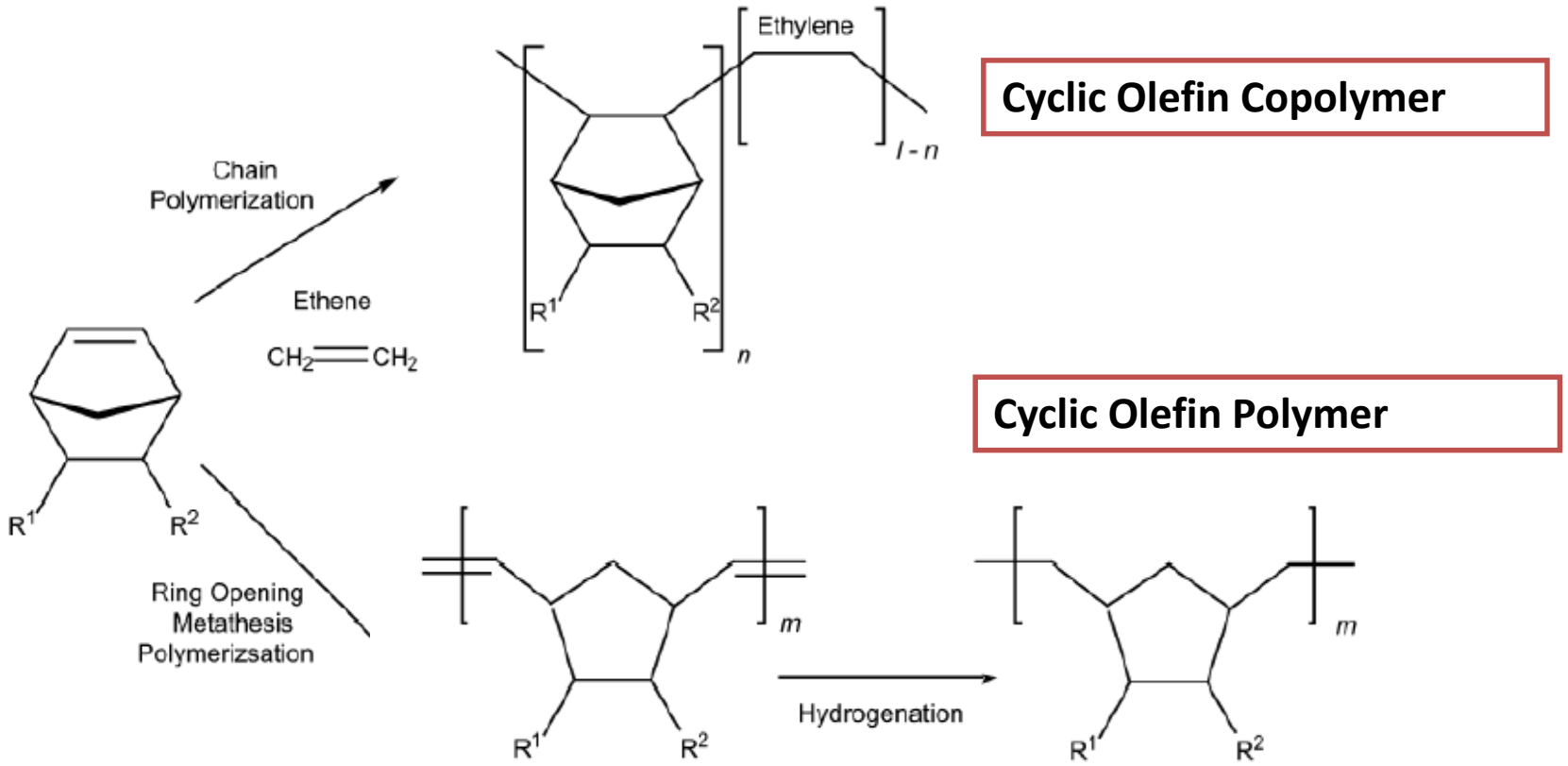
Cyclic Olefin Copolymer (COC)
and
Cyclic Olefin Polymer (COP)

- **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

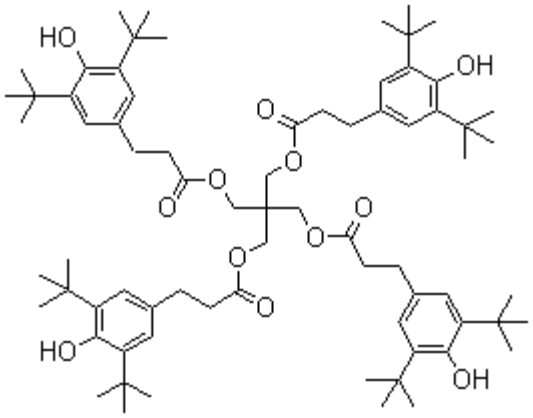


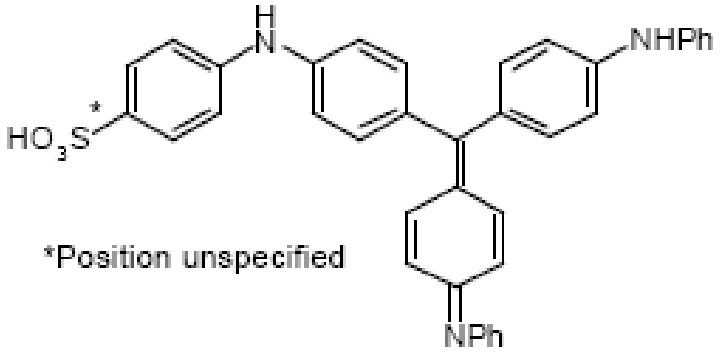
Non limitative list

Materials for Syringe Systems: Polyolefines

Stabilizer : Irganox 1010

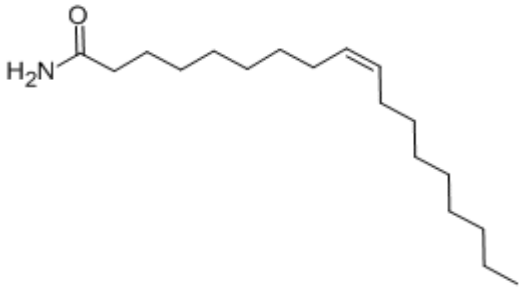
Pentaerythritol Tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate)





Colorant: Ultramarine Blue

Slip additives: Oleamide, Erucamide



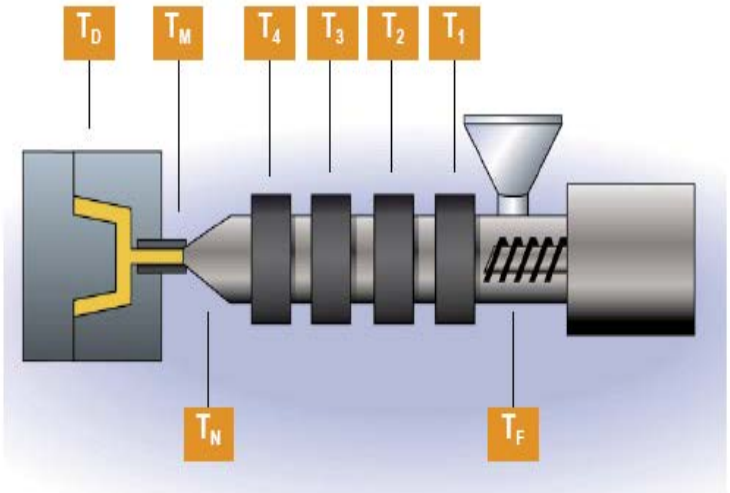
Materials for Syringe Systems: Polyolefines

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 °C T_1=230-260 °C T_2=240-270 °C T_3=250-280 °C T_4=260-290 °C T_N=240-300 °C T_M=240-300 °C
Mold-temperature:	T_D = 95 – 130 °C
Max. residence time	< 15 min; short interruption to cycle: reduce T_x= 170°C !
Injection pressure:	P_{Sp} = 500 - 1100 bar (specific)
Hold on pressure:	P_N = 300 - 600 bar (specific)

Back pressure:	P_{St} = 150 bar max. (specific)
Screw speed:	n_s = 50 - 200 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

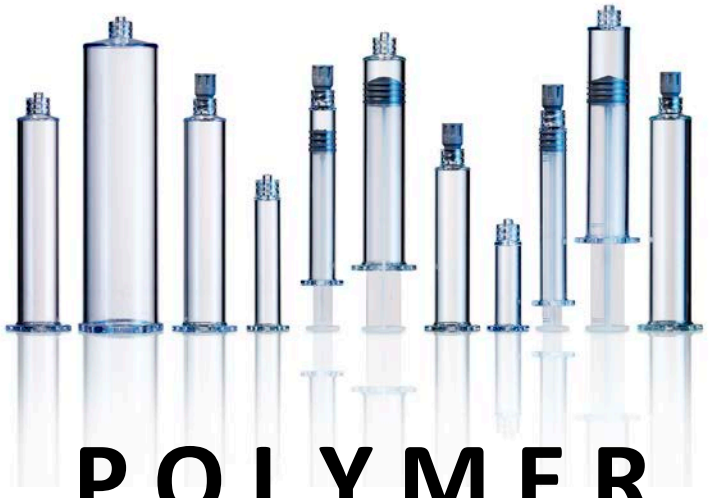
Company	Resin	Brand
Becton Dickinson	COP	BD Sterifill™ SCF™
Gerresheimer Taisei Kako	COP	ClearJect™
Schott Schweiz	COC	SCHOTT TopPac®
SiO_2 Medical Products	COP	Barrier Coated Systems
Terumo	COP	Playjex™
West (Daikyo)	COP	CZ® RU system

Non limitative list

What Material is the BETTER Choice ?

G L A S S

vs.



P O L Y M E R

Non limitative list

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		👍

Non limitative list

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)	👍	👍

Non limitative list

Advantages and Disadvantages of Materials

Polymer	Vs.	Glass

Vs.

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

Non limitative list

Sterilization Methods

Method	COC/COP	Glass
Autoclave 121° C, 20 min[1)]	yes	yes
Gamma irradiation, 25 kGy[2)]	yes	*no*
Electron radiation[2)]	yes	*no*
X-Ray[2)]	yes	*no*
Heat tunnel 280° C, 5 min	*no*	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

Non limitative list

Rubber Components for PFS

Major Suppliers for PFS Rubber Components

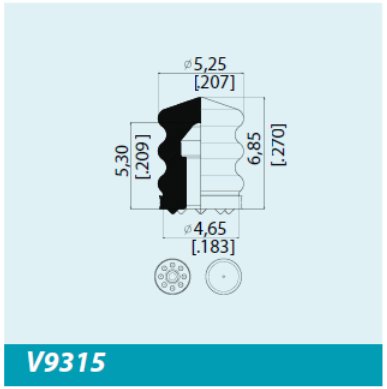
1. **Aptar Stelmi:** http://www.aptar.com/pharma/injectables/
2. **Datwyler:** http://sealing.datwyler.com/de/industry-solutions/health-care.html
3. **West:** http://www.westpharma.com/en/Pages/Default.aspx

Non limitative list

Rubber Components for PFS

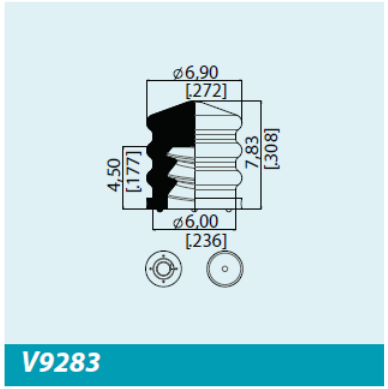
TYPICAL PRODUCTS

0.5 ml



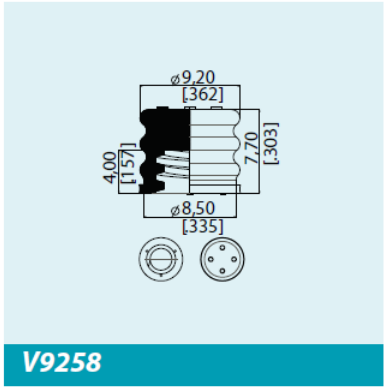
V9315

1 ml long



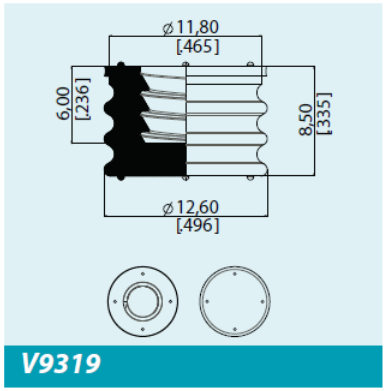
V9283

1 - 3 ml



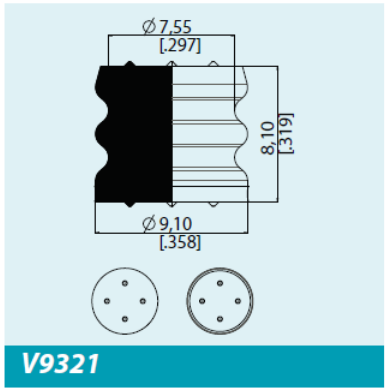
V9258

5 ml



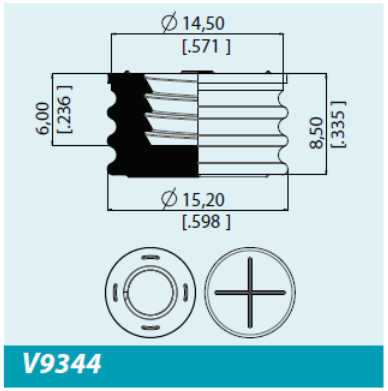
V9319

Dual chamber plunger



V9321

10 ml

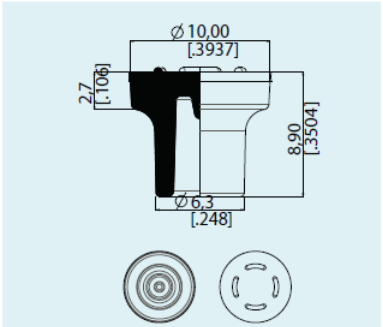


V9344

Drawings taken from Datwylers product brochures

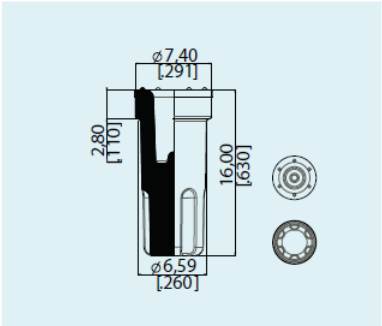
Rubber Components for PFS

Mushroom Tip Cap



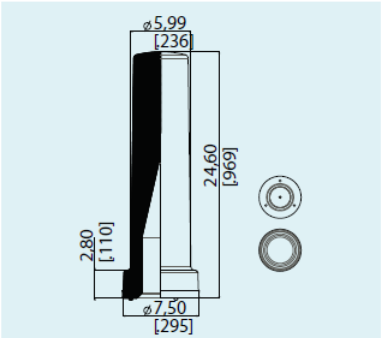
V9257

Ribbed Tip Cap



V9406

1/2" Needle Shield



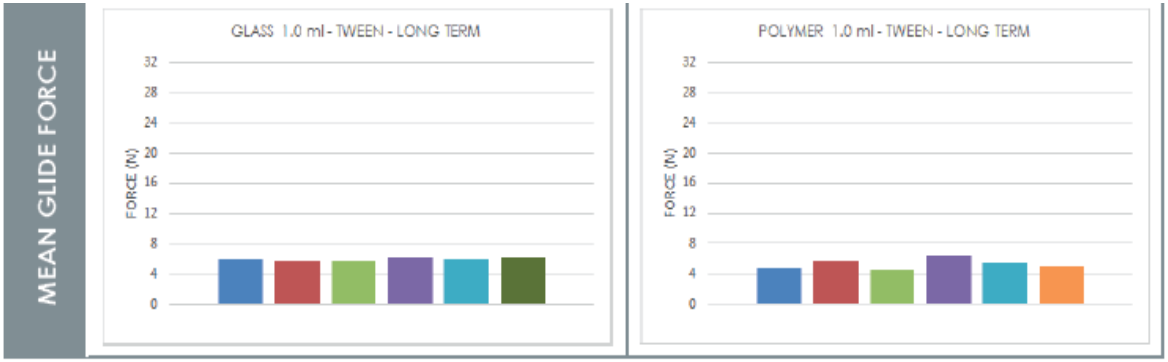
V6524

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 VI70ºC
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 ?