Best Practices for Glass Primary Containers

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Part I: Manufacture and Characteristics of Glass as Primary Packaging Material

Part II: Receiving Inspection of Glass Primary Packaging Material

Part III: Machine Use of Glass Primary Packaging Material

Part I: Manufacture and Characteristics of Glass as Primary Packaging Material

Glass Science

- Chemical Structure
- Physical Properties
- Different Glass Types
- Glass surface

Glass Making

- Melting & Tube drawing
- Container conversion
- Molded containers production process

Glass Strength & Fracture Mechanics: Dr. Florian Maurer

- Glass Breakage - Fundamentals
- Assessment of Flaws
- Fractography – Fundamentals

Visit SCHOTT Tubular Glass Manufacturing

Glass Science

Chemical Structure
Physical Properties
Different Glass Types
Glass surface

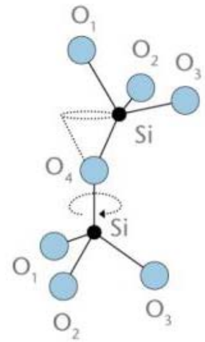
Question: What is glass?

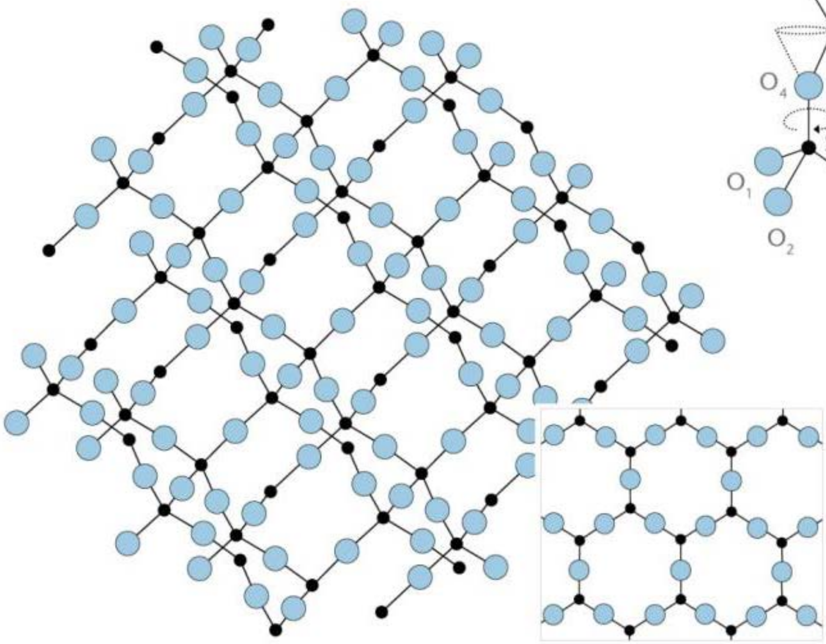
Answers

- Tamman (1932): Solid, non-crystalline materials are in the glass state
- Uhlmann (1972): Glasses are amorphous material with a crystalline fraction
- Scholze (1988): Glass is a frozen supercooled liquid

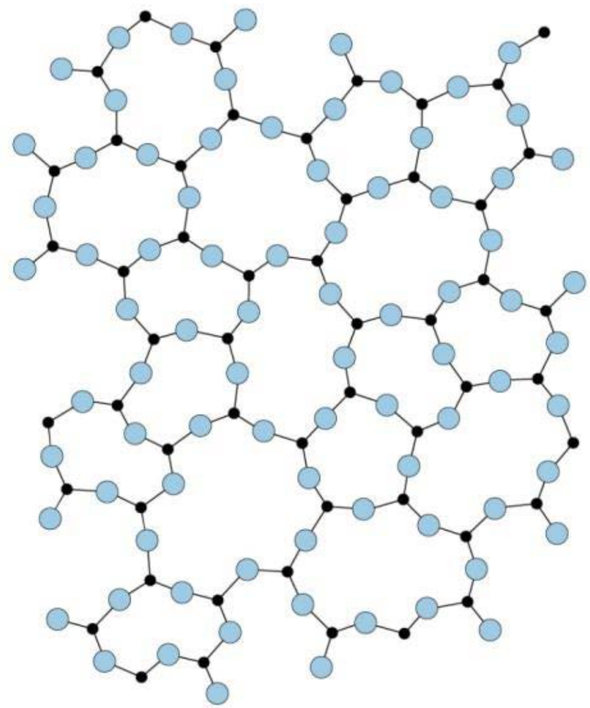
Chemical Structure

crystalline quartz
opaque crystal



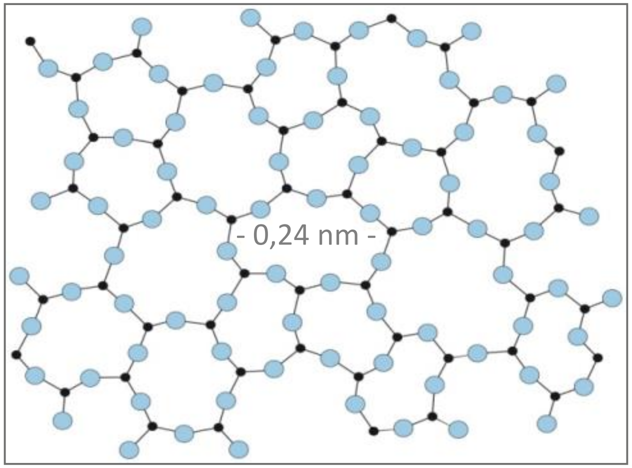


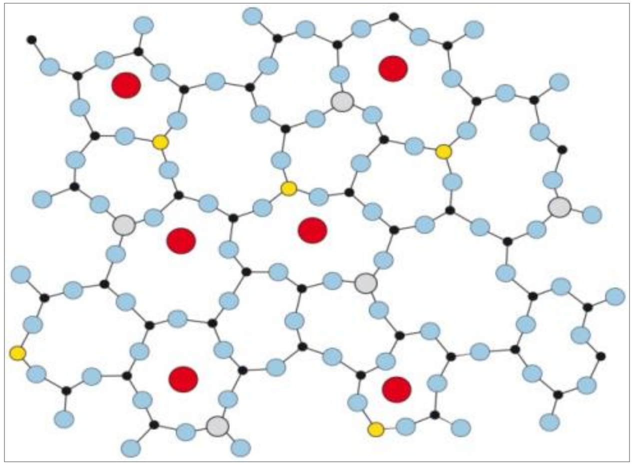
amorphous quartz
transparent glass

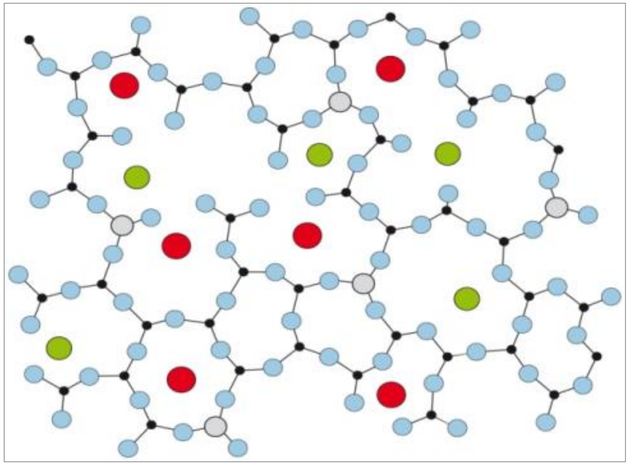


Chemical Structure

Amorphous silica	Borosilicate glass	Soda lime glass







chemical resistance

- Oxygen
- Silicon
- Boron

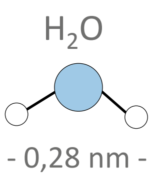
Network formers

- Sodium
- Calcium

Network modifiers

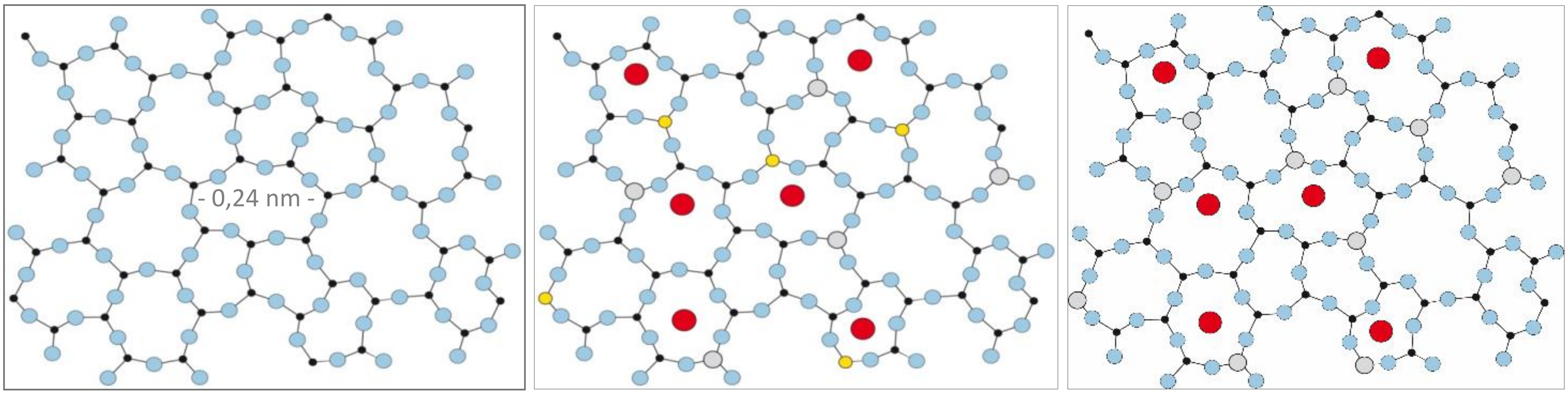
- Oxygen
- Silicon
- Boron
- Sodium
- Calcium
- Aluminum
- Hydrogen

Alkali metals
e.g. Na, K
Alkaline earth metals:
e.g. Ca, Ba, Mg



Chemical Structure

Amorphous silica | Borosilicate glass | Aluminosilicate glass



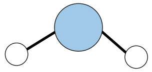
chemical resistance

- Oxygen, Silicon, Boron — Network formers
- Sodium, Calcium — Network modifiers

- Oxygen
- Silicon
- Boron
- Sodium
- Calcium
- Aluminum
- Hydrogen

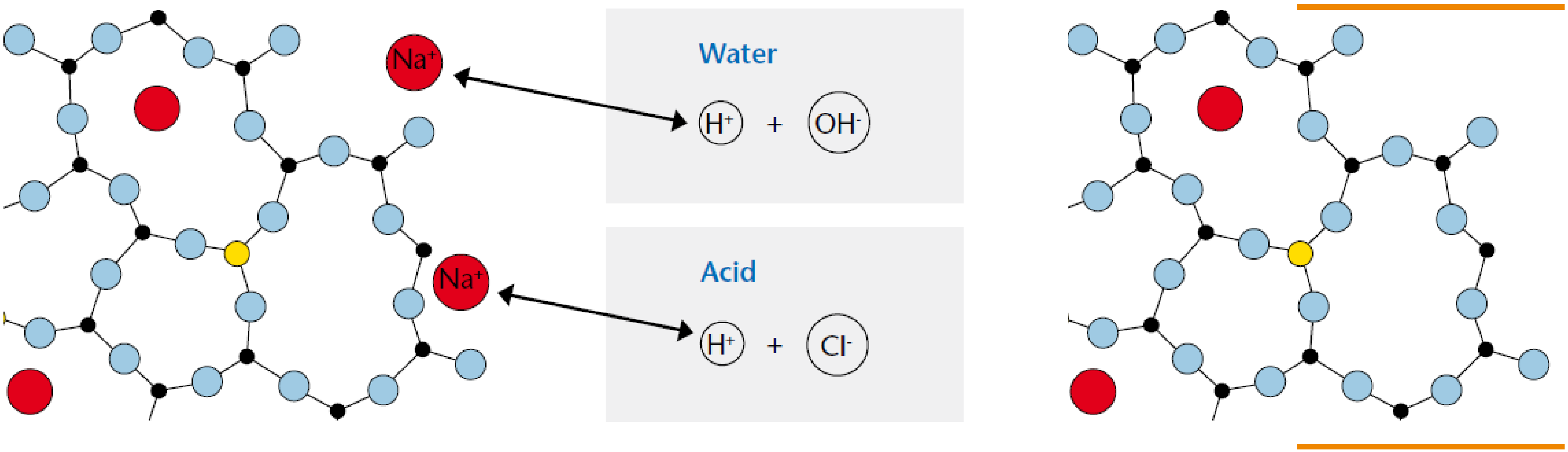
Alkali metals
e.g. Na, K
Alkaline earth metals:
e.g. Ca, Ba, Mg

H_2O

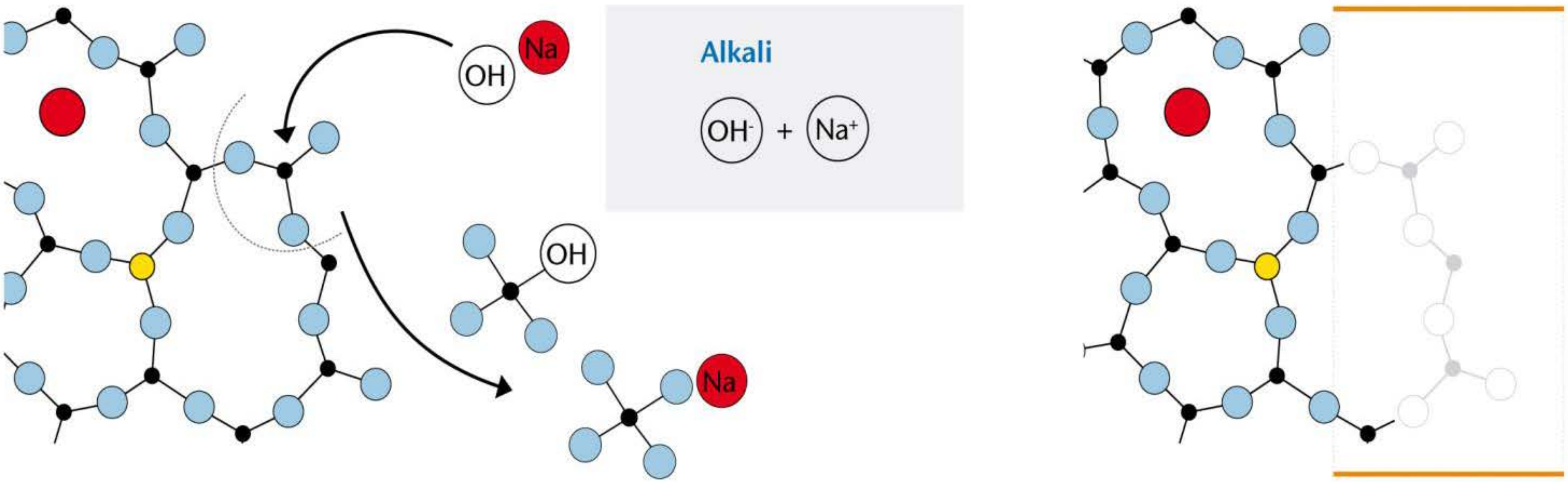


- 0,28 nm -

Chemical stability is the resistance of the glass to chemical attack by defined agents: Water and acid attack cause an ion exchange



Chemical stability is the resistance of the glass to chemical attack by defined agents: Alkali attack causes a dissolution of the network

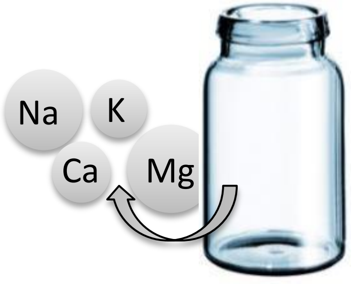


The quality of a glass is assessed by its hydrolytic stability

According to Ph. Eur. the hydrolytic stability is defined as follows:

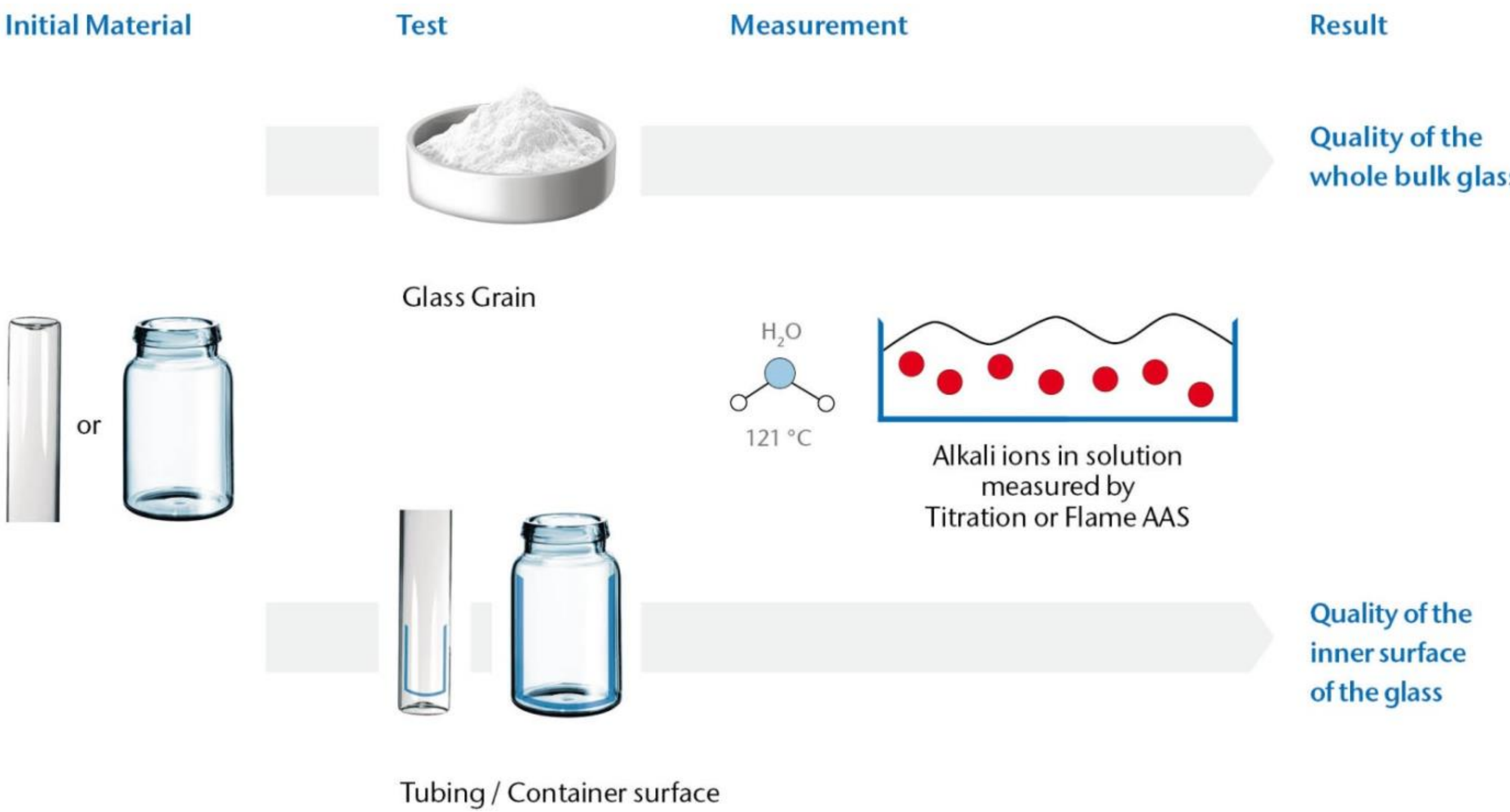
The hydrolytic stability of glass containers for pharmaceutical use is expressed by the resistance to the release of soluble mineral substances into water under the prescribed conditions of contact between the **inner surface** of the container or **glass grains** and water.

Soluble mineral substances can be: Na, K, Ca, Ba, Mg



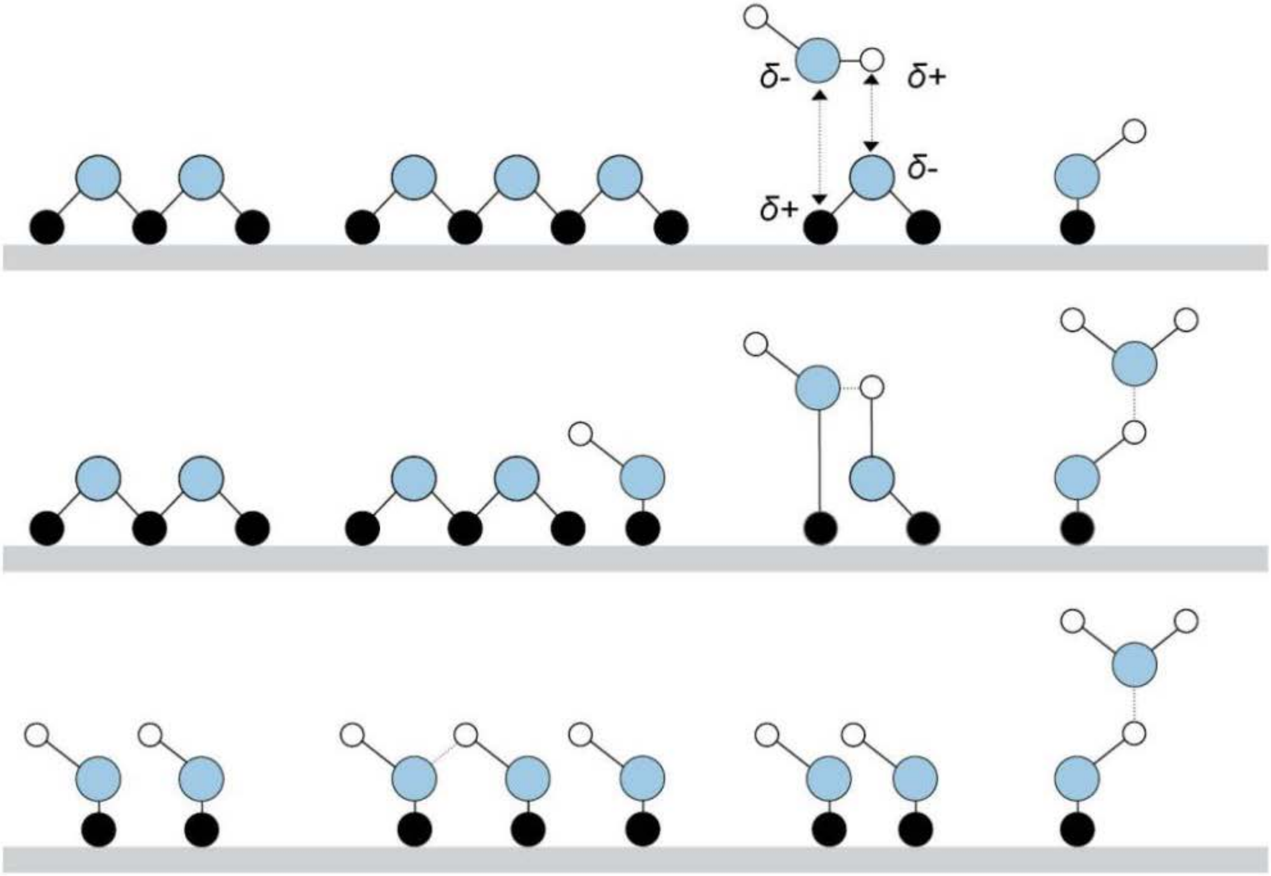
Chemical Structure – Hydrolytic resistance

Two methods to determine the glass quality – principle



Chemical Structure – Water skin

The protection layer evaporates easily but builds up very slowly again

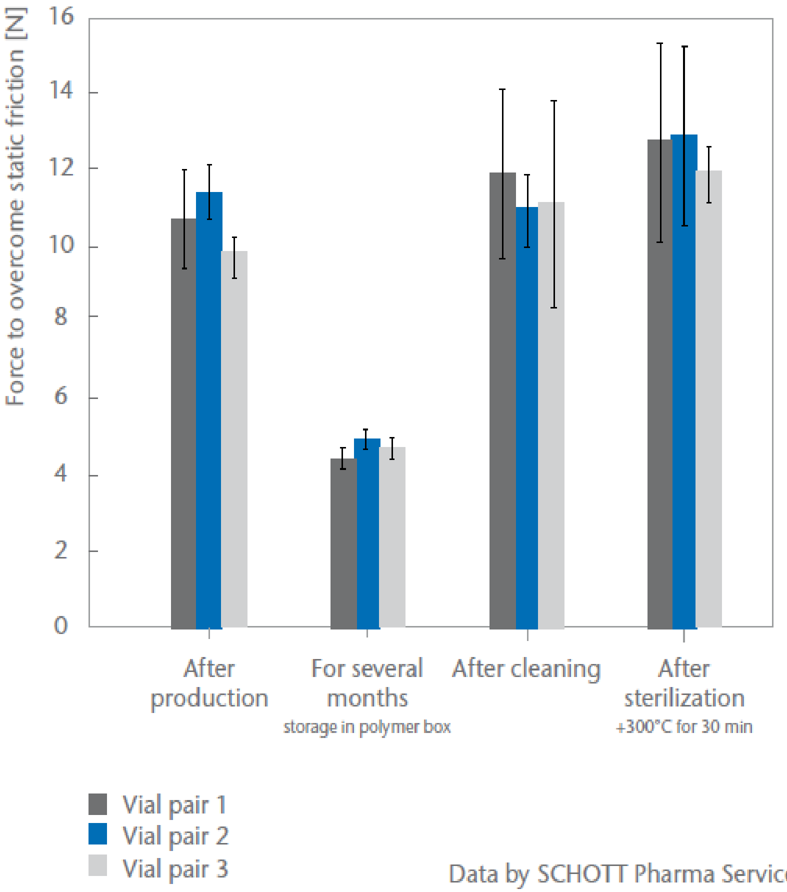


Hot glass surface:
Scratch sensitive!

Adsorption of humidity
during cooling
(air contact, coating)

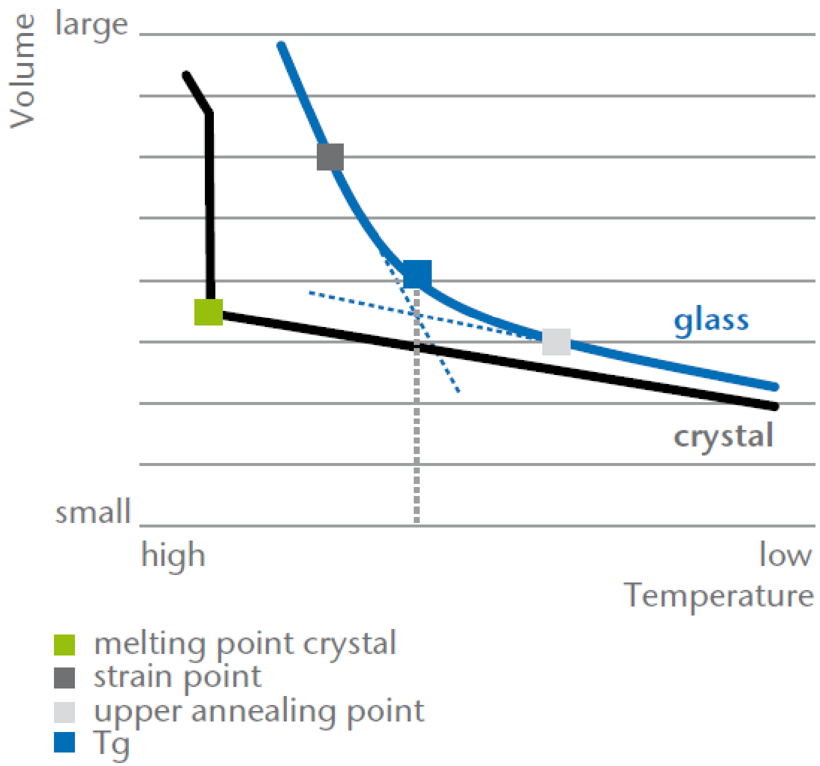
Saturated glass surface
„water skin"
- Better scratch resistance

Friction measurements prove the existence of the protection layer



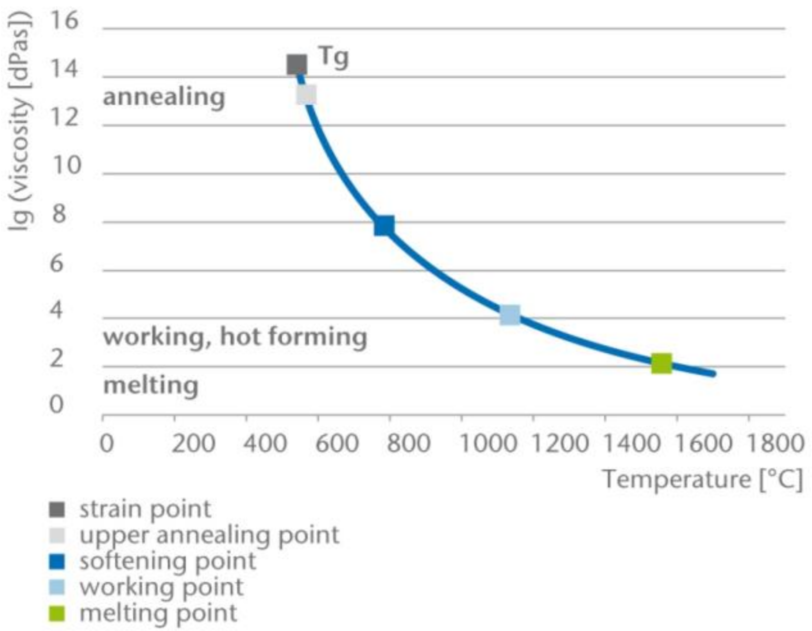
Data by SCHOTT Pharma Service

Glass behaves differently from other materials like e.g. water/ice
The solidification curve is smooth and shows no crystallization point



Physical Properties - Viscosity

Viscosity is the resistance to flow.
The higher the resistance the higher the viscosity.



	Viscosity η (dPas)
Water	10^{-2}
Honey	10^{2}
Glass melt (1600 °C)	10^{2}
Glass at Tg (550 °C)	$10^{13,5\text{-}14,5}$
Glass at RT (25 °C)	10^{19}

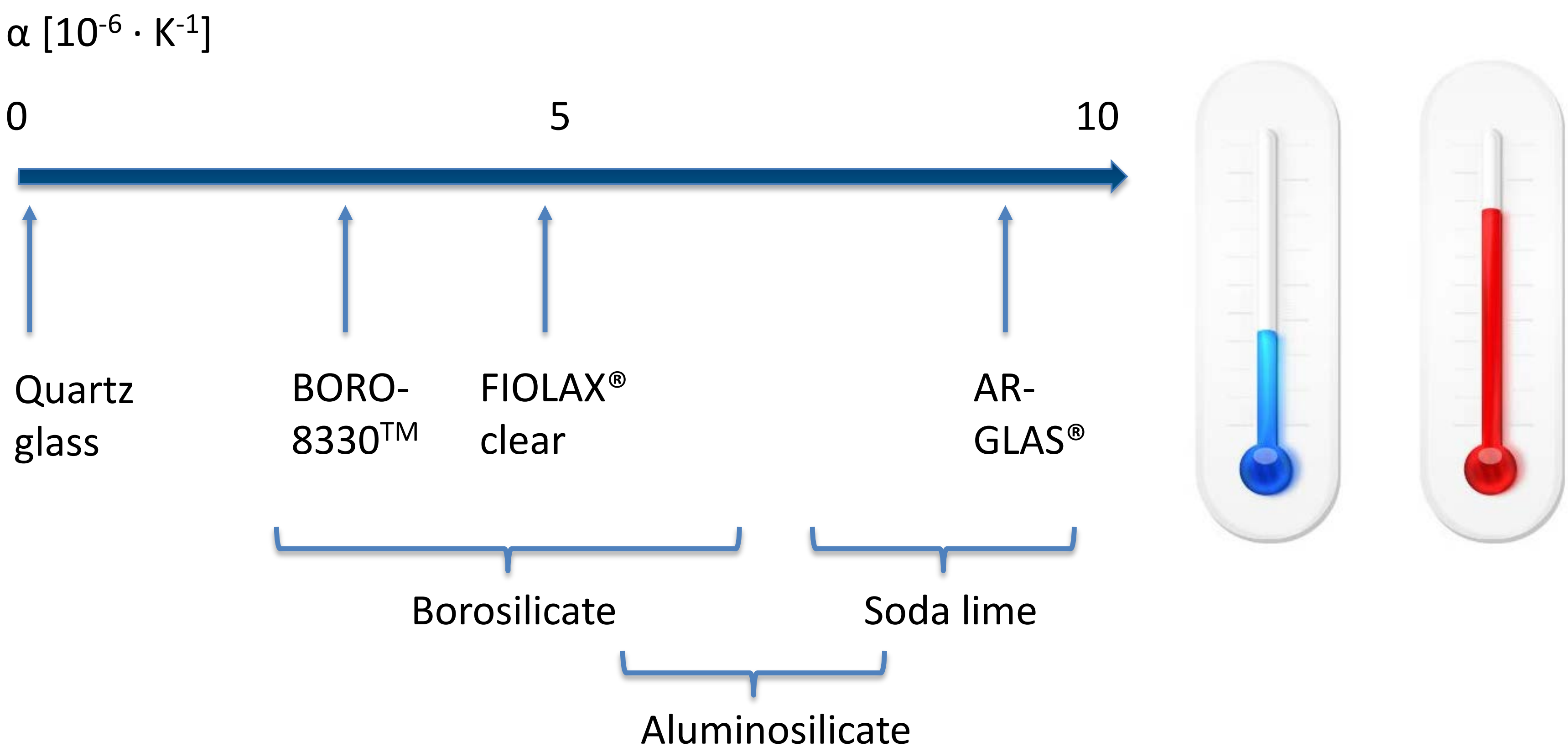
FIOLAX® clear

Technical Data

Glass Type/Application	Neutral glass tubing, chemically highly resistant Pharmaceutical primary packaging		
Physical Data	Coefficient of mean linear thermal expansion α (20°C;300°C) acc. to ISO 7991	4.9	$10^{-6}K^{-1}$
	Transformation Temperature T_g	565	°C
	Glass temperature at viscosity η in dPa·s		
	10^{13} (annealing point).....................................	565	°C
	$10^{7.6}$ (softening point)	785	°C
	10^{4} (working point)..	1160	°C
	Density ρ at 25°C	2.34	$g \cdot cm^{-3}$

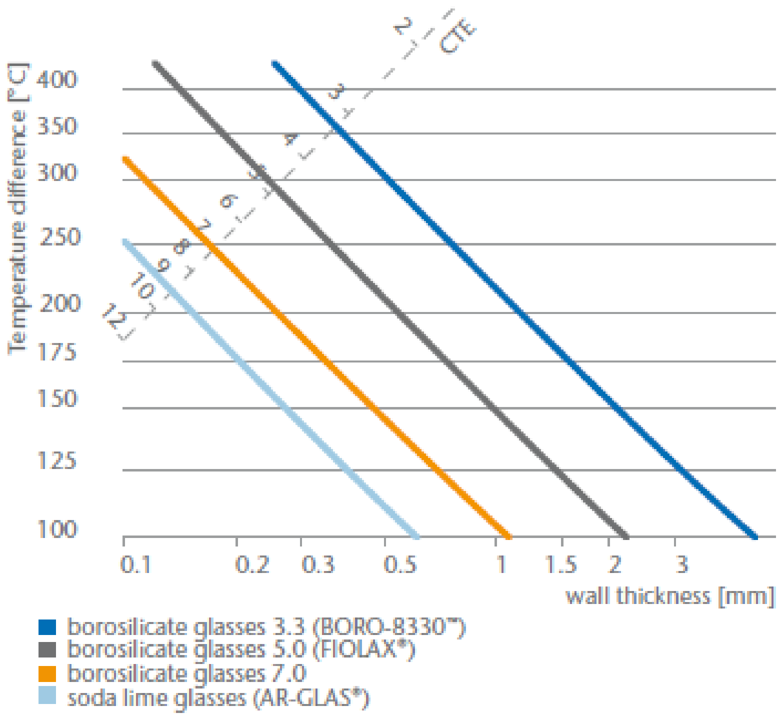
Physical Properties – Thermal Expansion

The coefficient of thermal expansion (CTE or α) describes how much a material expands when it is heated. The smaller the CTE the less it expands.



Physical Properties – Thermal Shock Resistance

Glass has a very low thermal conductivity. The thermal shock resistance depends on both the CTE and the wall thickness.

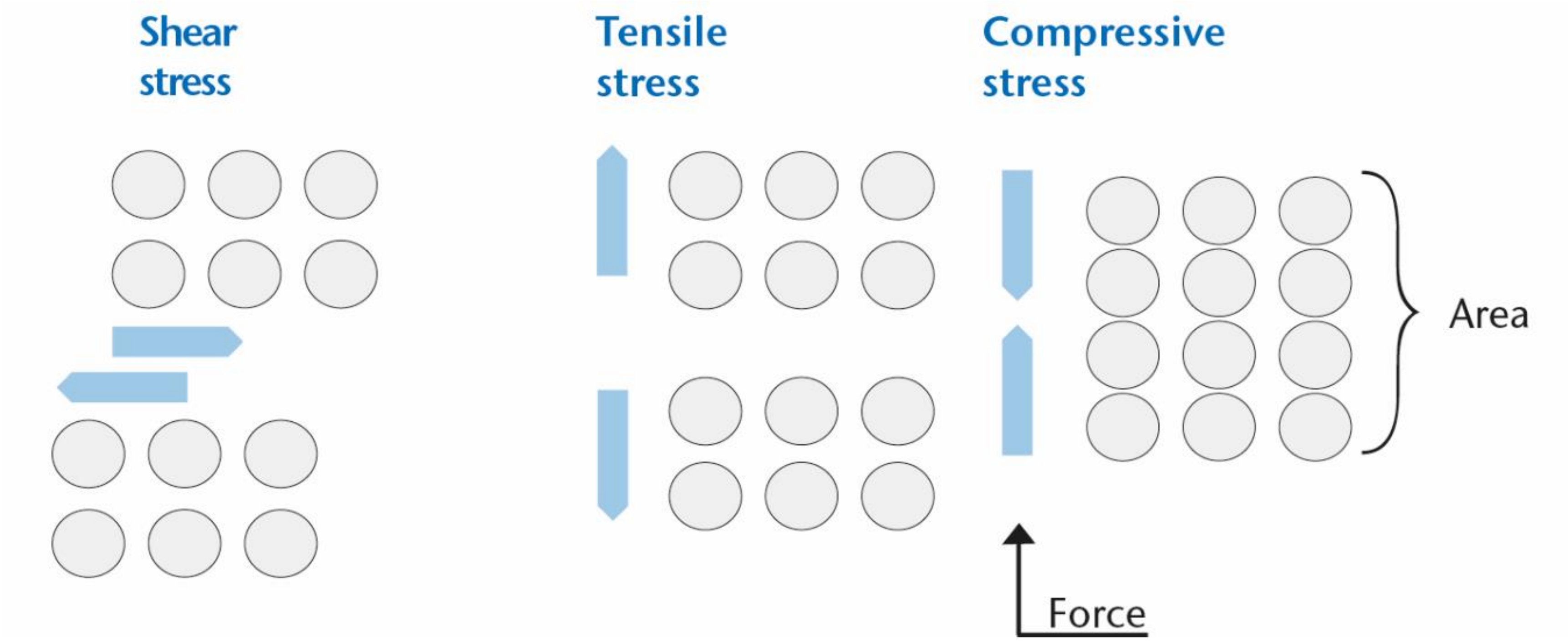


The smaller the CTE the higher the thermal shock resistance.

The thinner the wall the higher the thermal shock resistance.

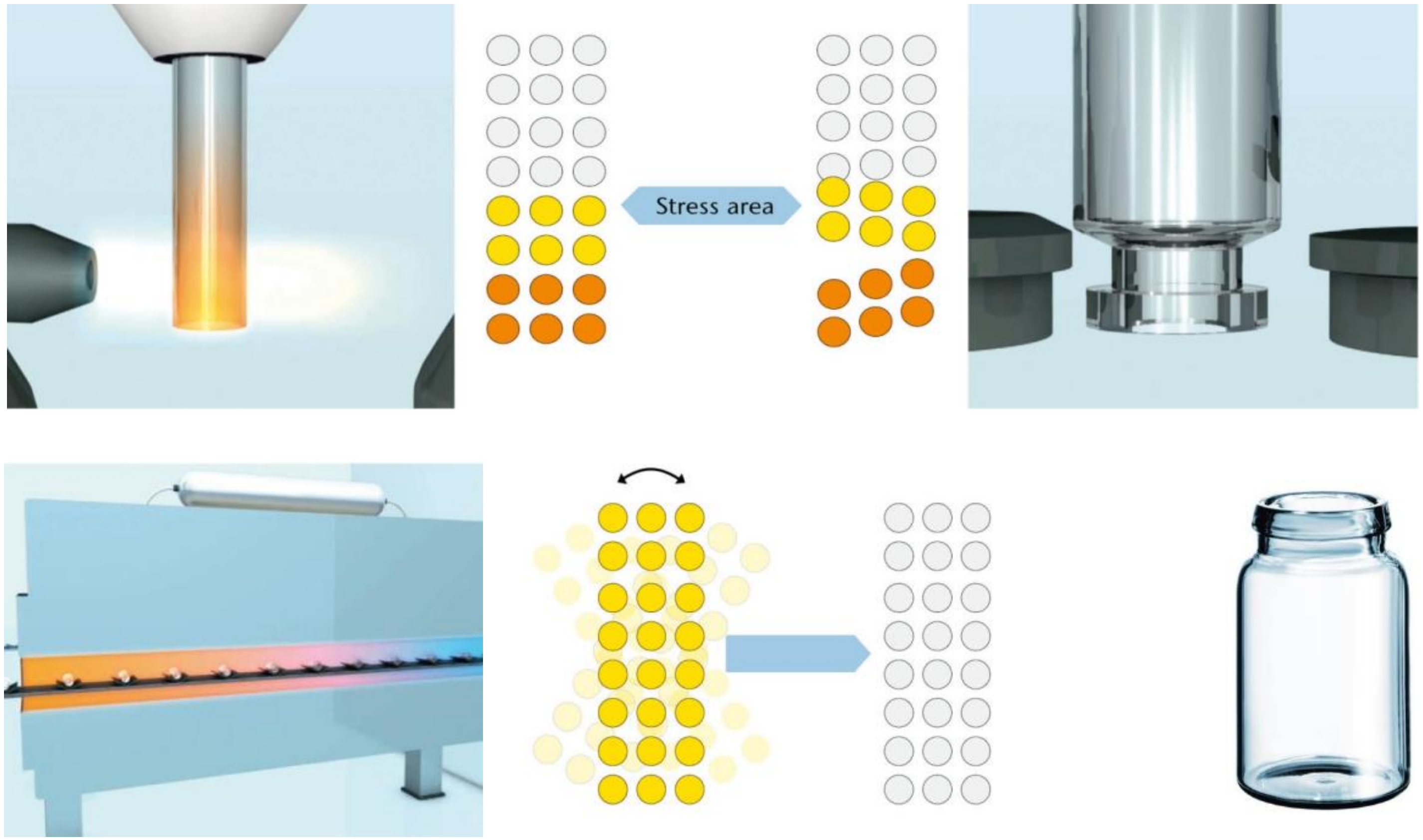
Physical Properties - Stress

Stress is defined as force per area.
There are three kinds of stresses described for glass:



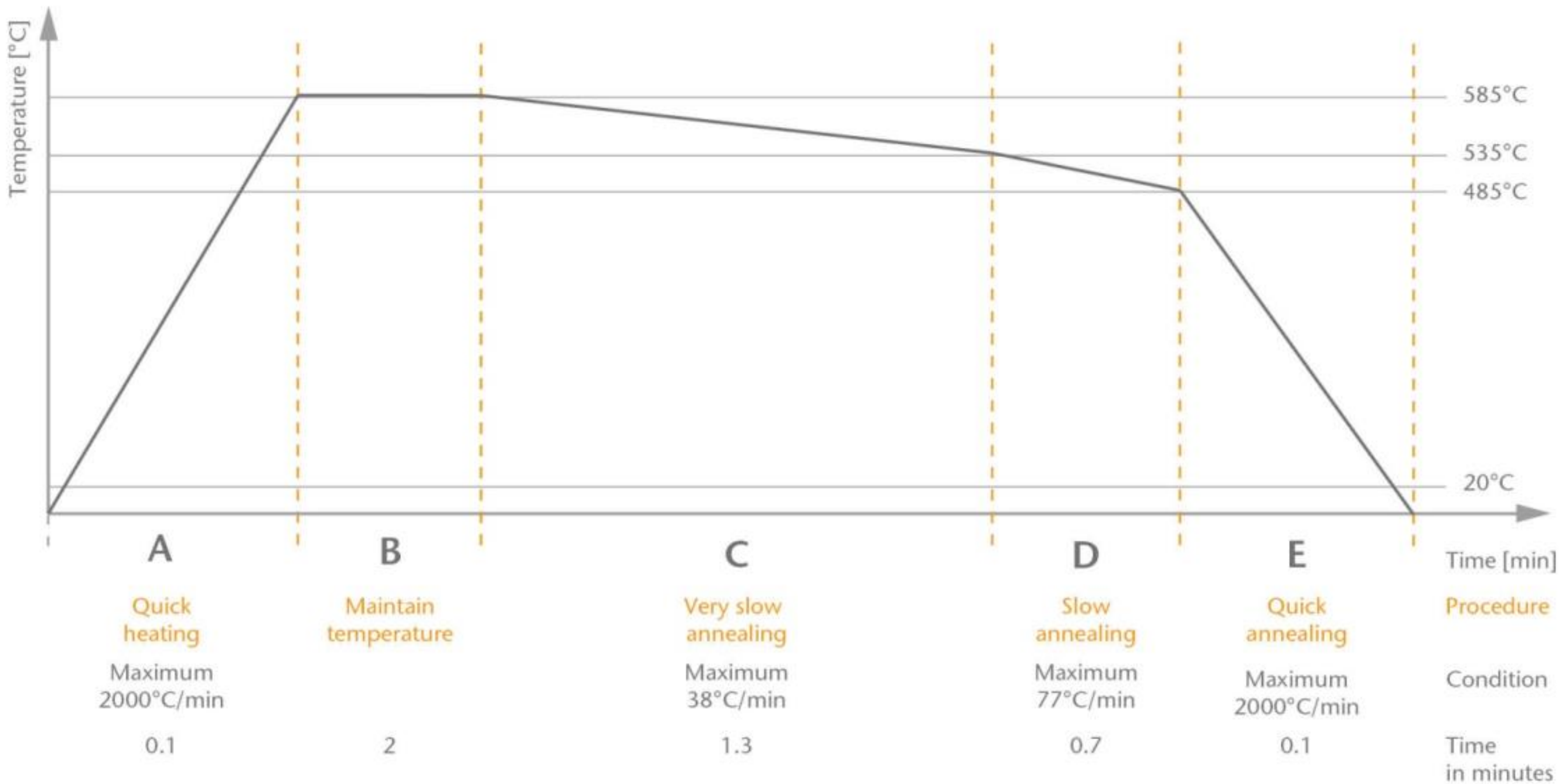
Physical Properties - Stress

Stress is created by partial quick cooling from temperatures above Tg.
It can only be released when heating above Tg and cooling down slowly.



Typical annealing curve for release of residual stress

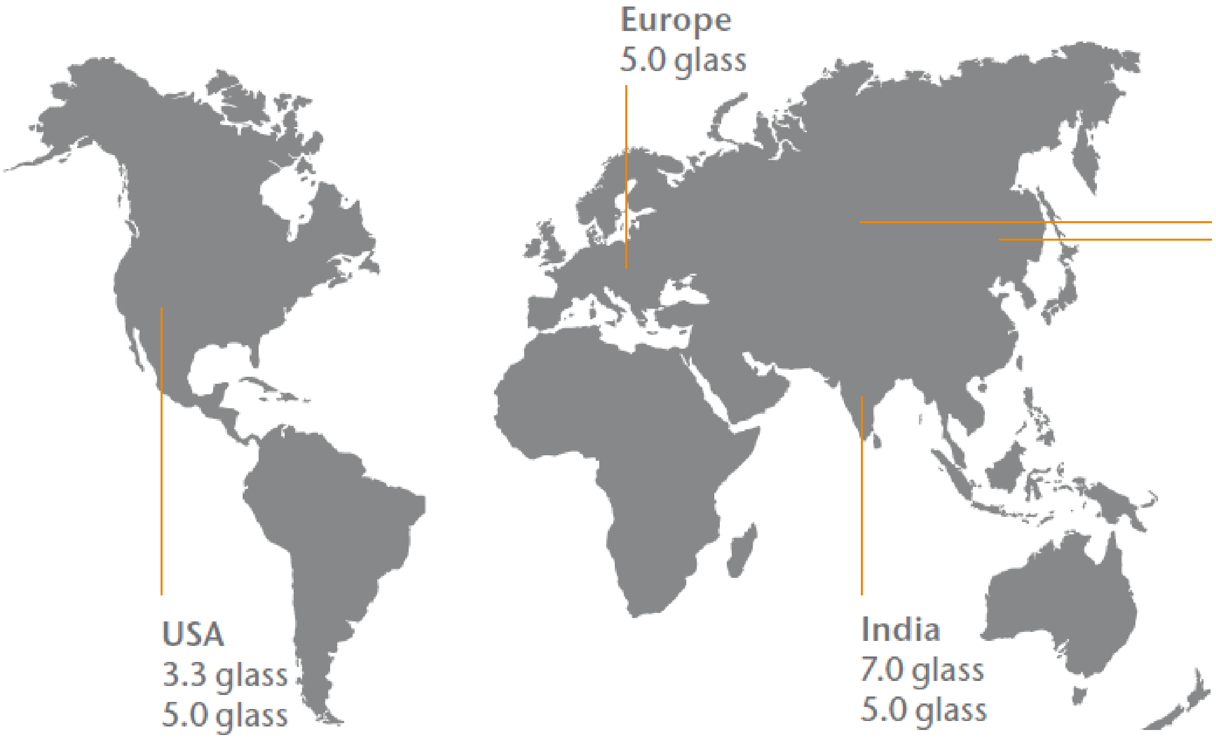
Annealing curve for FIOLAX® clear for a wall thickness of 1 mm



Different Glass Types – within the Borosilicate Group

There are 3 groups of Type I glass tubing

- 3.3 glass is mainly used in the USA.
- 5.0 glass („FIOLAX® type“, neutral glass) is the most widely used pharmaceutical glass worldwide.
- 7.0 glass is mainly used in India, China, Russia.



Different Glass Types – within the Borosilicate Group

Glass Type	Borosilicate 3.3	Borosilicate 5.0	Borosilicate 7.0
Composition			
SiO_2	80 - 82	72 - 75	70 - 74
B_2O_3	12 - 13	9 - 11	5 - 8
Al_2O_3	2	5 -7	4 - 6.5
Na_2O/K_2O	4	6 - 9	9 - 12
MgO/CaO/BaO	0	1 - 3	5 - 7
Physical Data			
Working Point	1,260 °C	1,145 - 1,170 °C	1,030 - 1,100 °C
Transformation Temperature (Tg)	525 °C	565 - 575 °C	550 - 580 °C
Mean Coefficient of Thermal Expansion (CTE)	3.3	4.9 - 5.5	6.3 - 7.5

Molded Tubing Molded Tubing

52 gramm 40 gramm

Different Glass Types

	Borosilicate 3.3 group tubing	Borosilicate 5.0 group tubing	Borosilicate 7.0 group tubing	Borosilicate Type I group molded	Soda lime glass
Composition					
SiO_2	80 - 82	72 - 75	70 - 74	65 - 70	70-75
B_2O_3	12 - 13	9 - 11	5 - 8	9 - 11	0 - 1
Al_2O_3	2	5 - 7	4 - 6,5	3 - 7	2 - 4
Na_2O/K_2O	4	6 - 9	9 - 12	9 - 10	12 - 16
MgO/CaO/BaO	0	1 - 3	5 - 7	4 - 5	10 - 15
Physical Data					
Working Point	1260°C	1145 - 1170°C	1030 - 1100°C	1050 - 1080°C	1015 - 1045°C
CTE	3.3	4.9 - 5.5	6.3 - 7.5	6.0 - 6.5	9 - 9.5

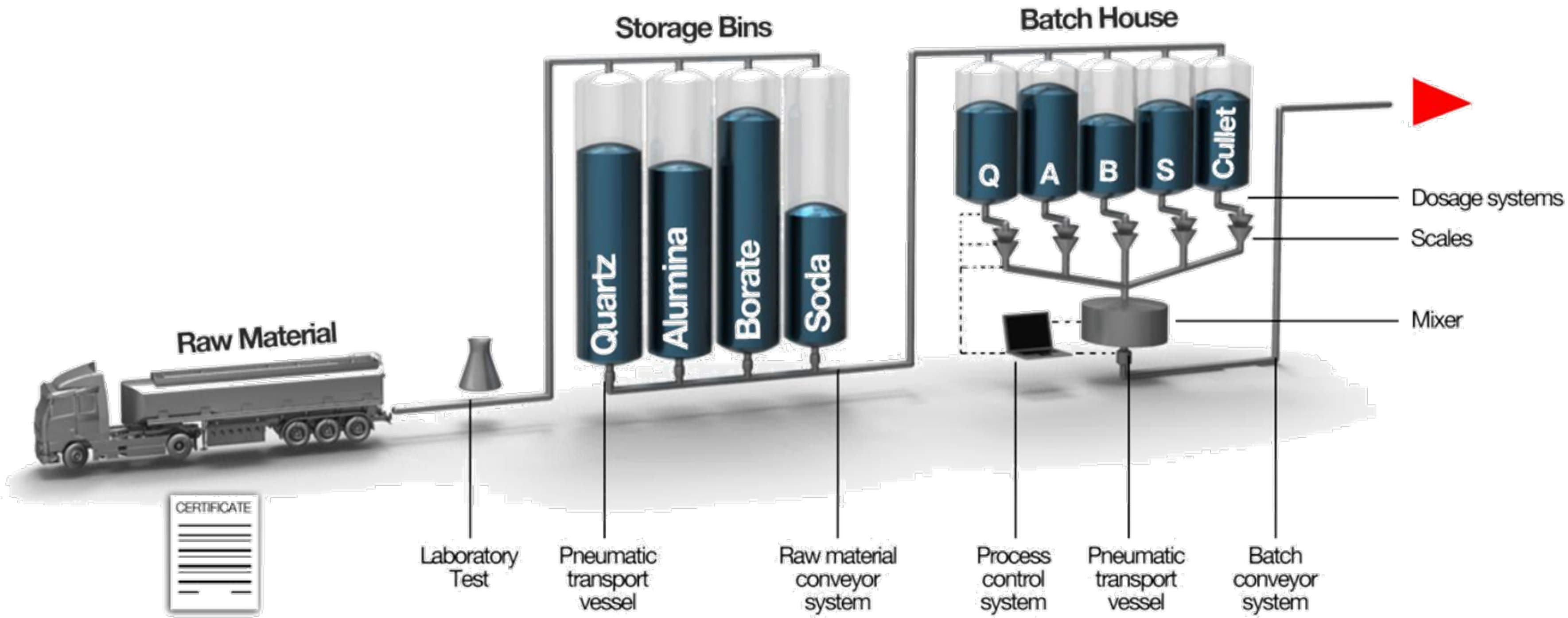
Glass Making

Melting & Tube drawing
Container conversion
Molded containers production process

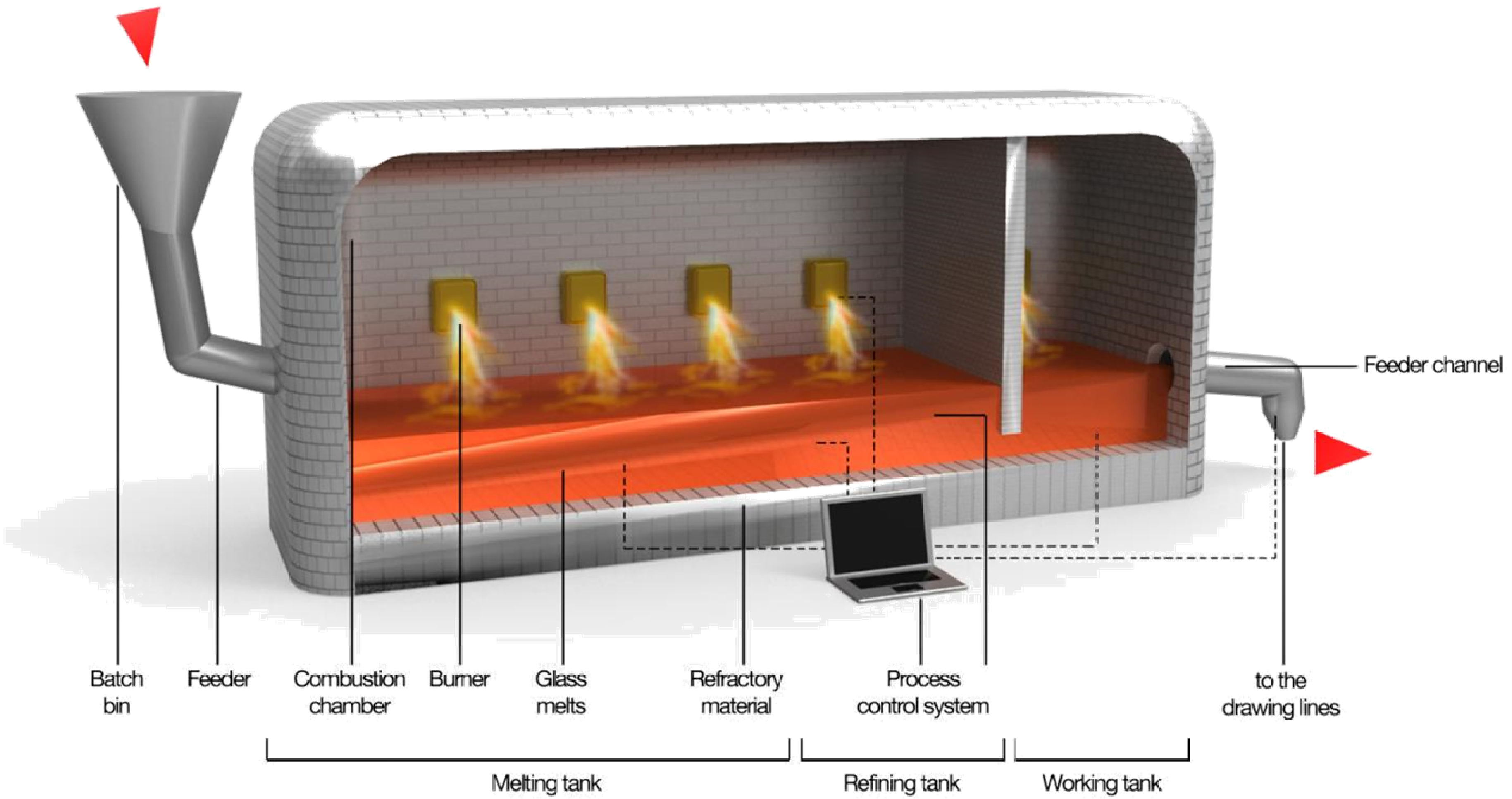
Melting & Tube Drawing

Element	Raw material as found in nature	
Network formers		
Silicon (Si)	SiO_2	sand
Boron (B)	$Na_2B_4O_7$	borax
Network intermediates		
Aluminum (Al)	Al_2O_3	alumina
Network modifiers		
Sodium (Na)	Na_2CO_3	soda
Potassium (K)	K_2CO_3	potash
Calcium (Ca)	$CaCO_3$ $CaMg(CO_3)_2$	chalk, marble, limestone dolomit
Magnesium (Mg)	$MgCO_3$ $CaMg(CO_3)_2$	magnesia dolomit

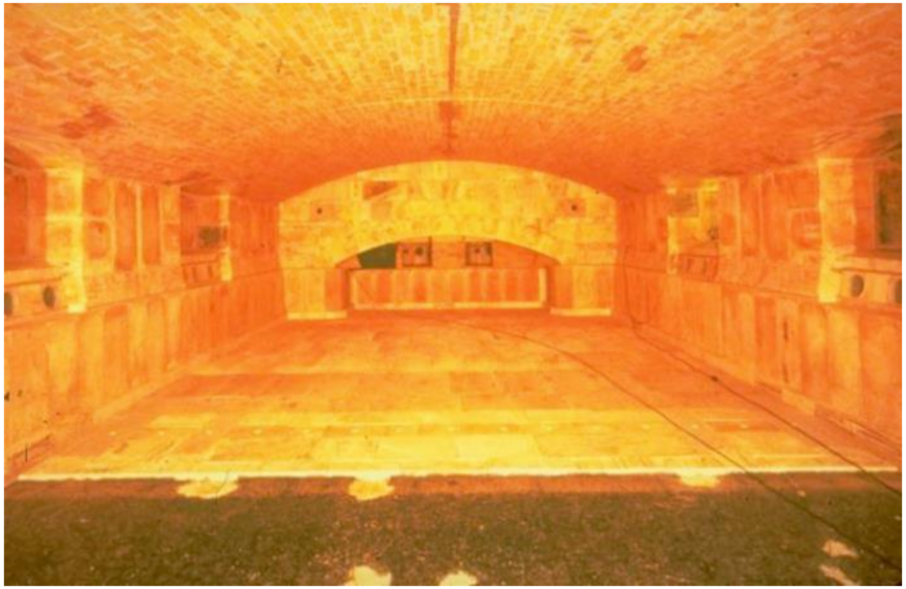
Melting & Tube Drawing



Melting & Tube Drawing



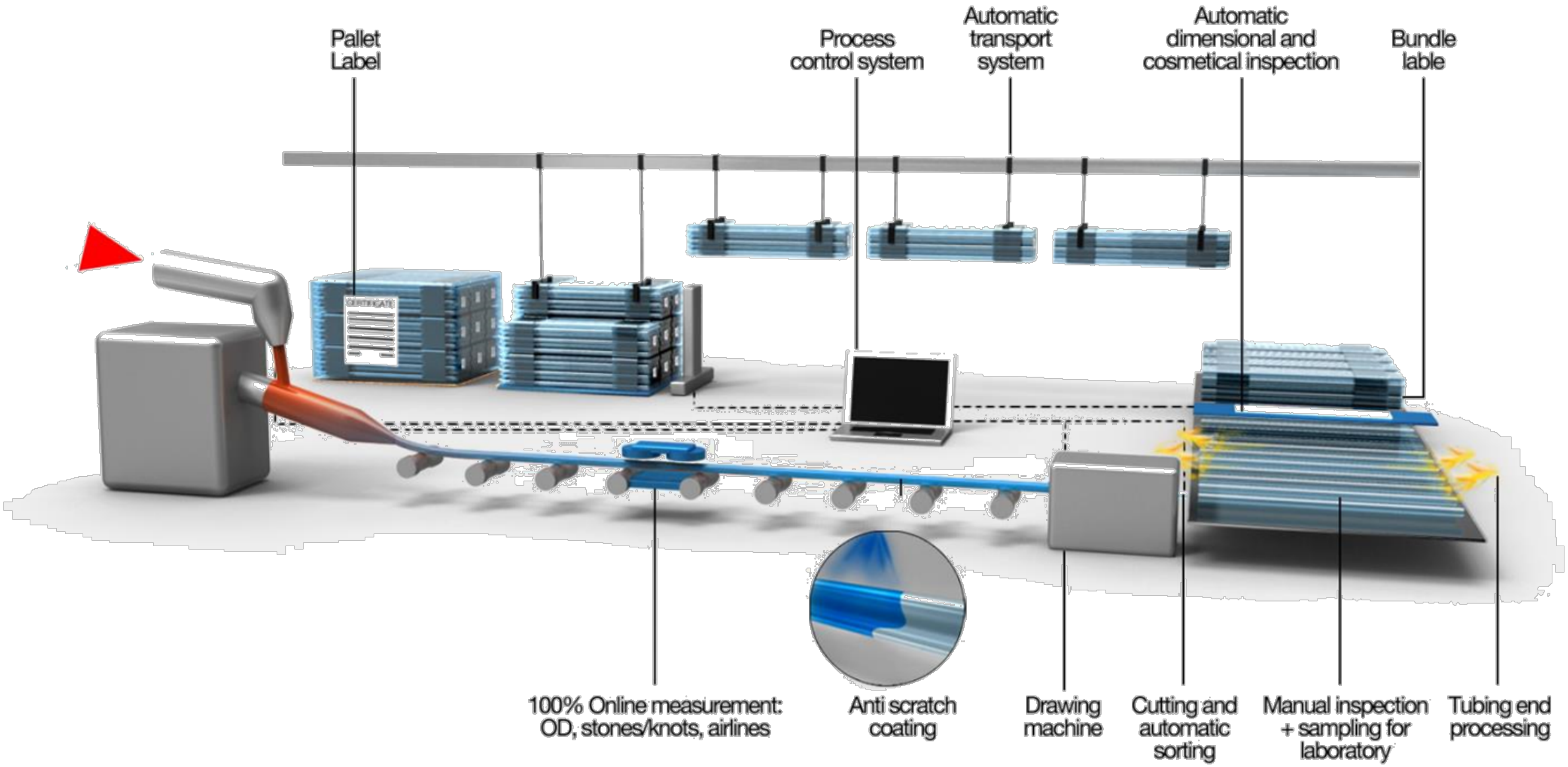
Melting & Tube Drawing



Melting tank

Danner mandrel

Melting & Tube Drawing



Surface Defects from Tubing: Stones and Knots

Stones: opaque inclusions

Knots: transparent inclusions

Source: Material that is not melted properly in the melting procedure

Stones

Knots

Surface Defects from Tubing:
Airlines

Closed: elongated gaseous inclusion within the glass

Open: elongated gaseous inclusion on the glass surface

Source: Gas created during the melting process and not removed properly

Surface Defects from Tubing: Scratches

Scratch: constitutes a slight damage to the outer surface of the glass but it does not penetrate the glass wall

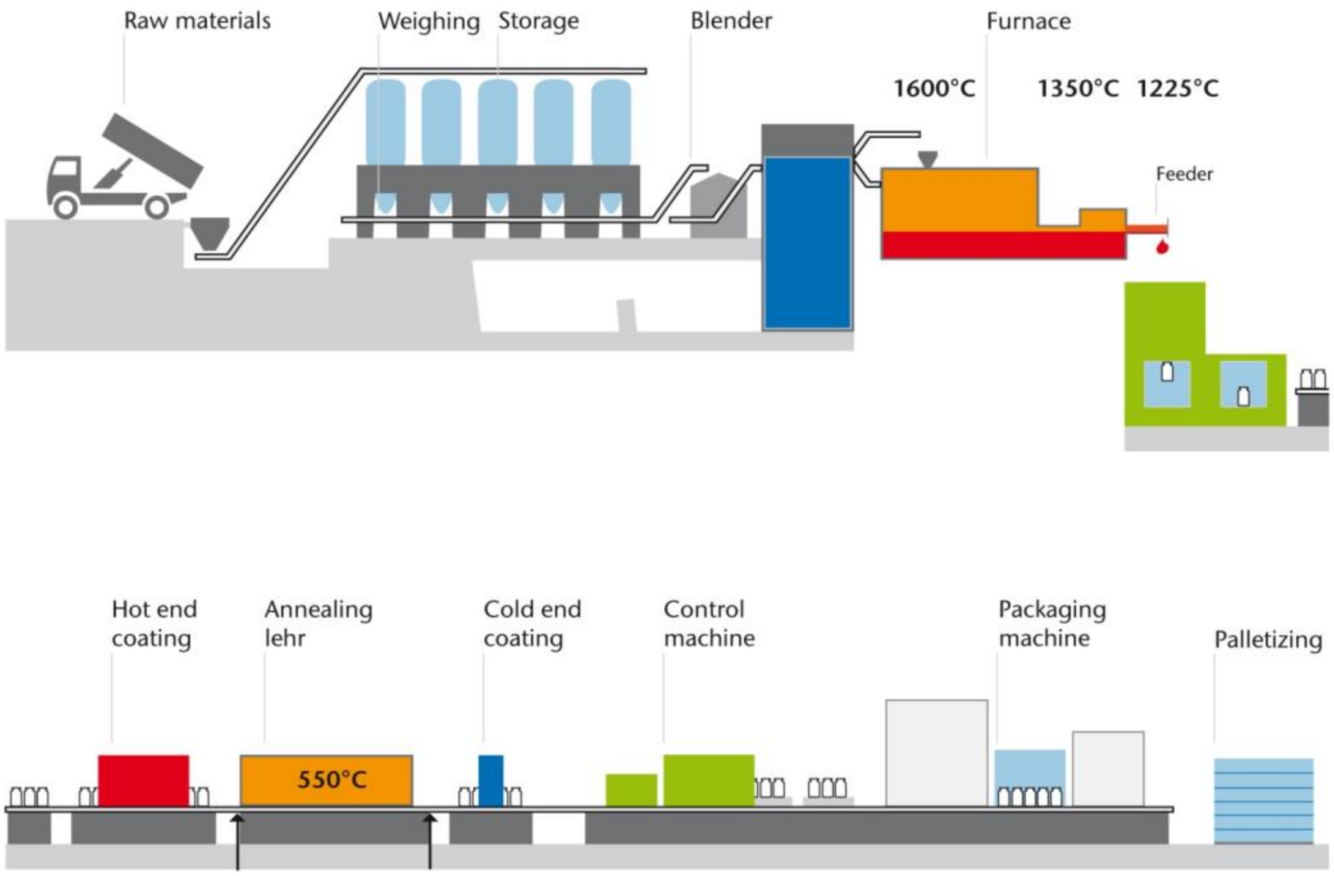
Source: A scratch can be created along the whole value chain

Movie Tubing Production

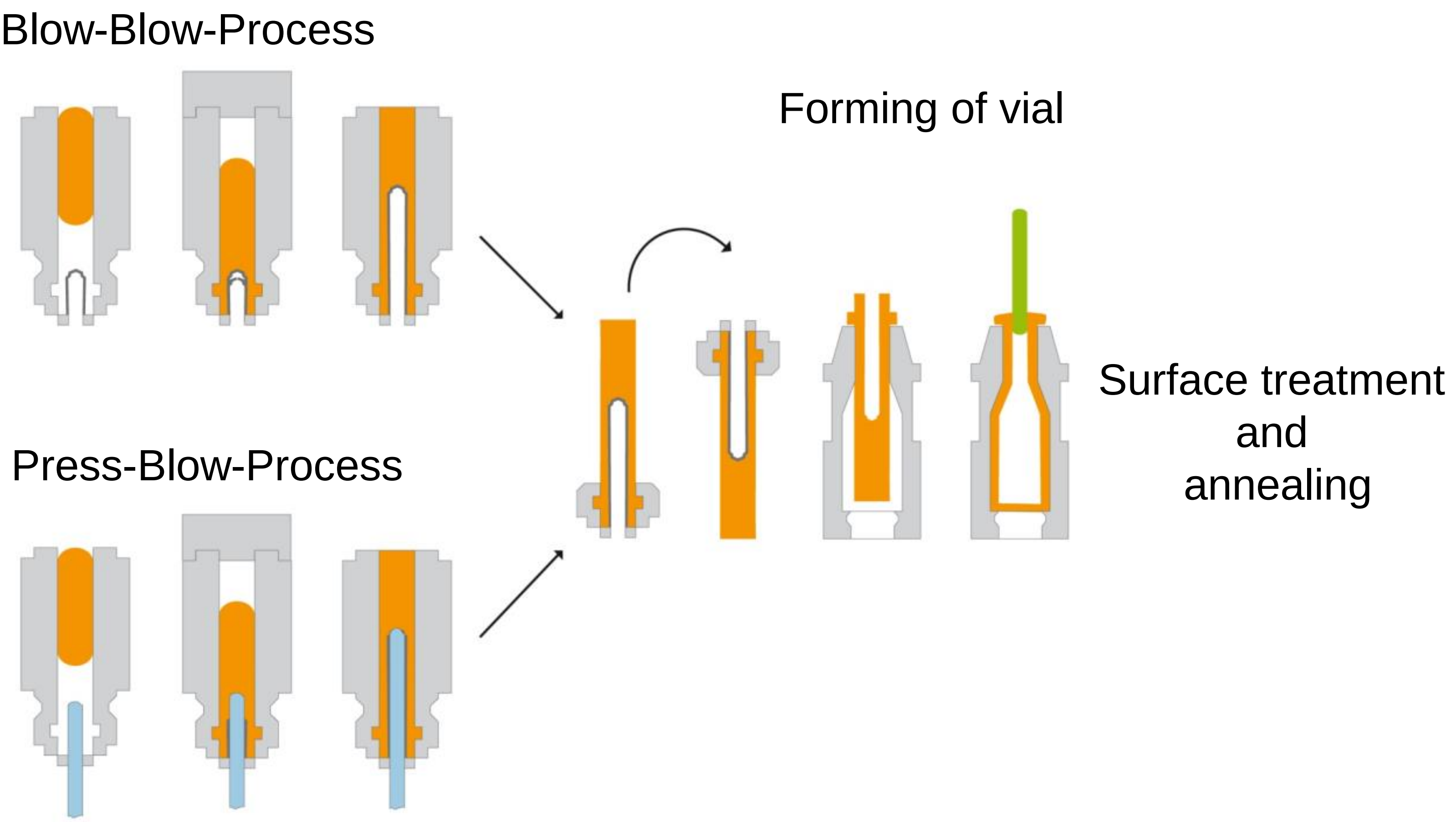
Movie Vial Production

Movie Syringe Production

Molded Containers Production Process



Molded Containers Production Process



Courtesy of SGD

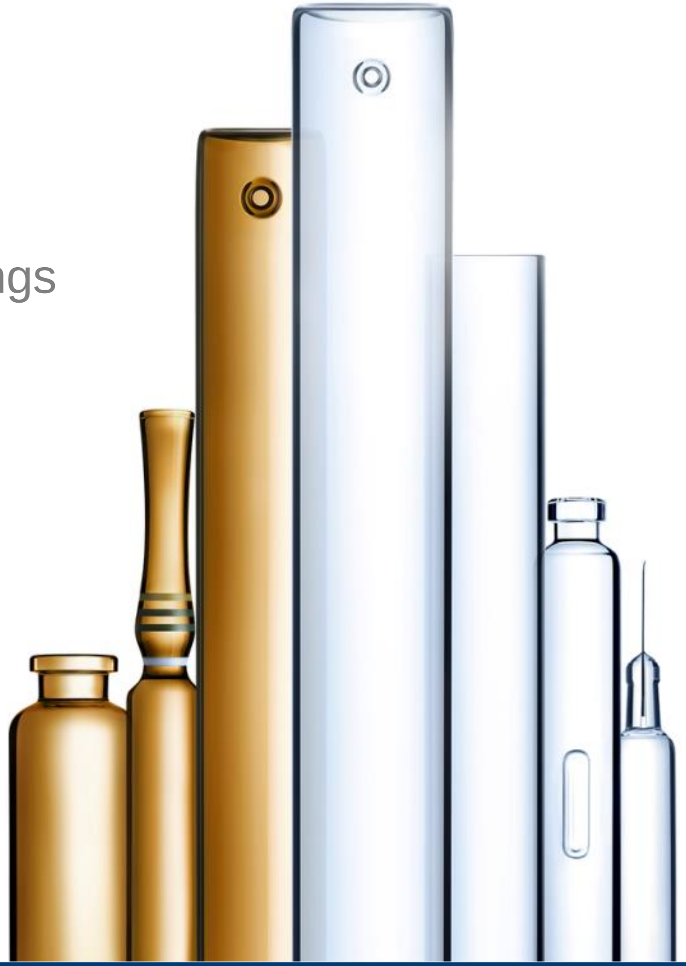
Further Treatments

Inner surface treatment

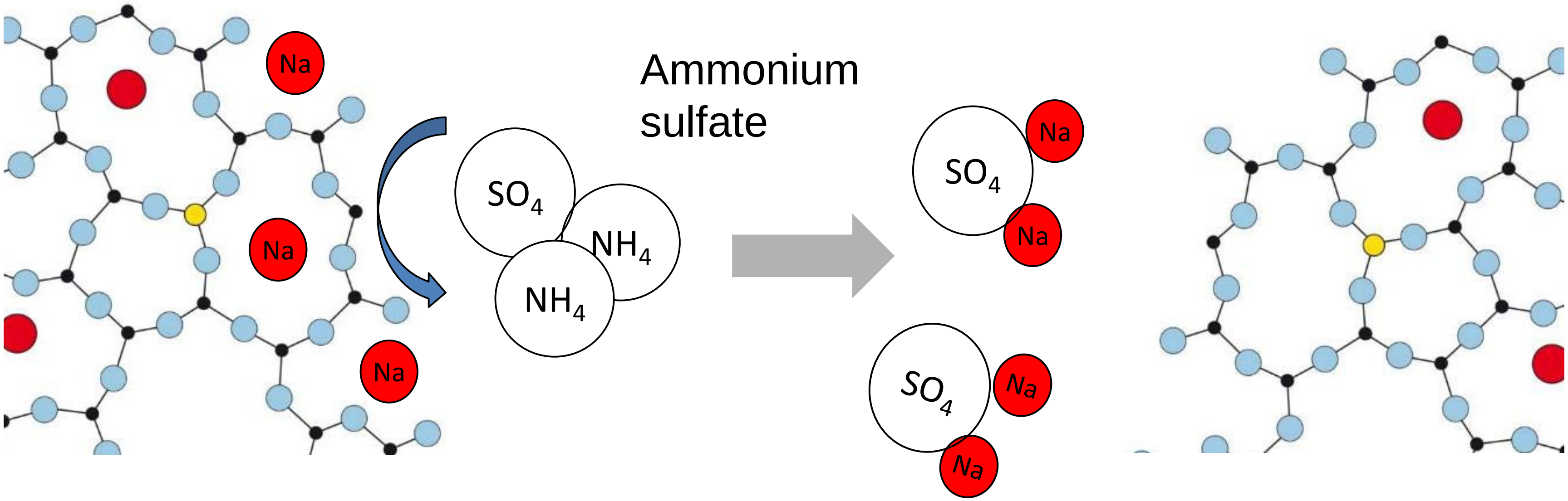
- Ammonium sulfate treatment
- Siliconisation of containers
- hydrophilic / hydrophobic coatings
- Chemical strengthening

Outer surface treatment

- Anti-scratch coating for tubing
- Siliconisation of vials and ampoules

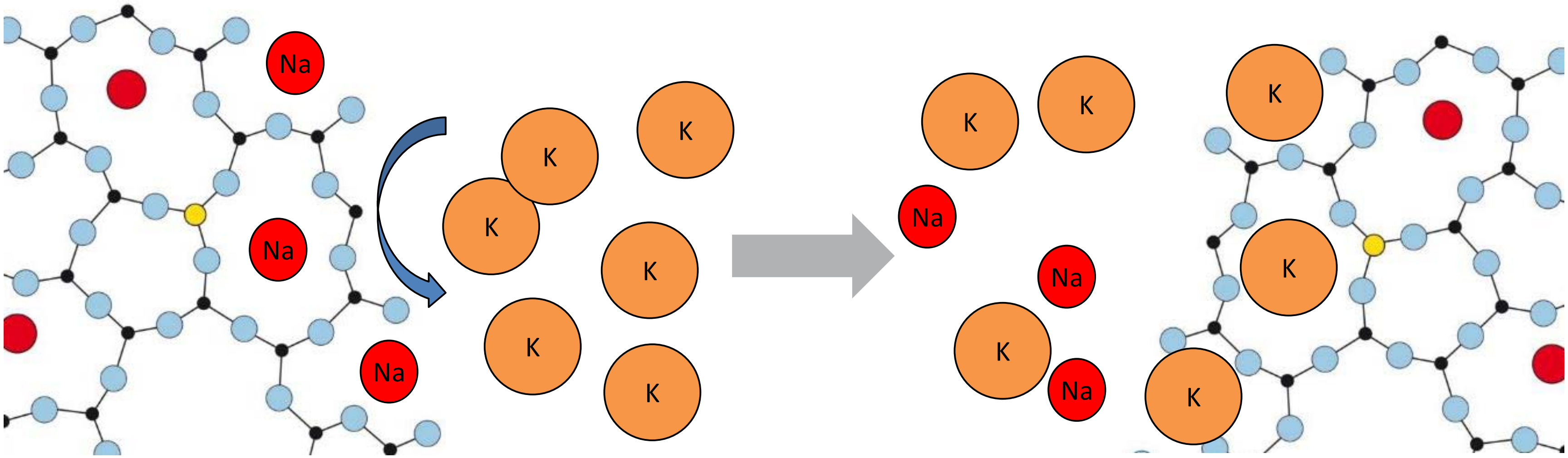


Further Treatments – Ammonium sulfate treatment



Increasing the hydrolytic resistance of the surface

BUT: compromising the surface integrity and increasing the risk of flake creation (Delamination)



Exchange of sodium by potassium ions creates compressive stress on the surface

Requires subsequent chemical treatment (leaching process) before use

Take-away messages

- Network: Glass consists of network formers (Si, O, B,…) as well as network modifiers (Na, K, Ca,…)
- Chemical Stability: the lower the amount of network modifiers the higher the chemical and hydrolytic resistance and the lower the interaction with the drug
- Regulatory: The hydrolytic resistance is measured by the glass grains test and the inner surface test → borosilicate glass is type I glass, sodalime glass is type III
- Thermal expansion: Glasses can be categorized acc. to their CTE (e.g. 5.0 borosilicate glass). The lower the CTE the higher the thermal shock resistance
- Stress: Local melting leads to internal stress and requires an annealing step
- Production: Glass can either be drawn in tubes and afterwards converted into containers (tubular vials, ampoules, syringes, cartridges) or blown into shape directly from the melt (molded vials)

Site Visit – Melting Tank

Smoking is generally forbidden inside of all buildings.

Be sure to watch for in-company traffic when entering transport routes. Use the marked walkways.

It is strictly forbidden to take photos or videos in our plant without permission.

The use of mobile phones is generally forbidden in the marked areas. It is strictly forbidden to connect electronic devices to the company network.

Thank you very much!

Claudia.Heinl@schott.com

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