

Machine Use of Glass Primary Packaging Material

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Pharma liquid



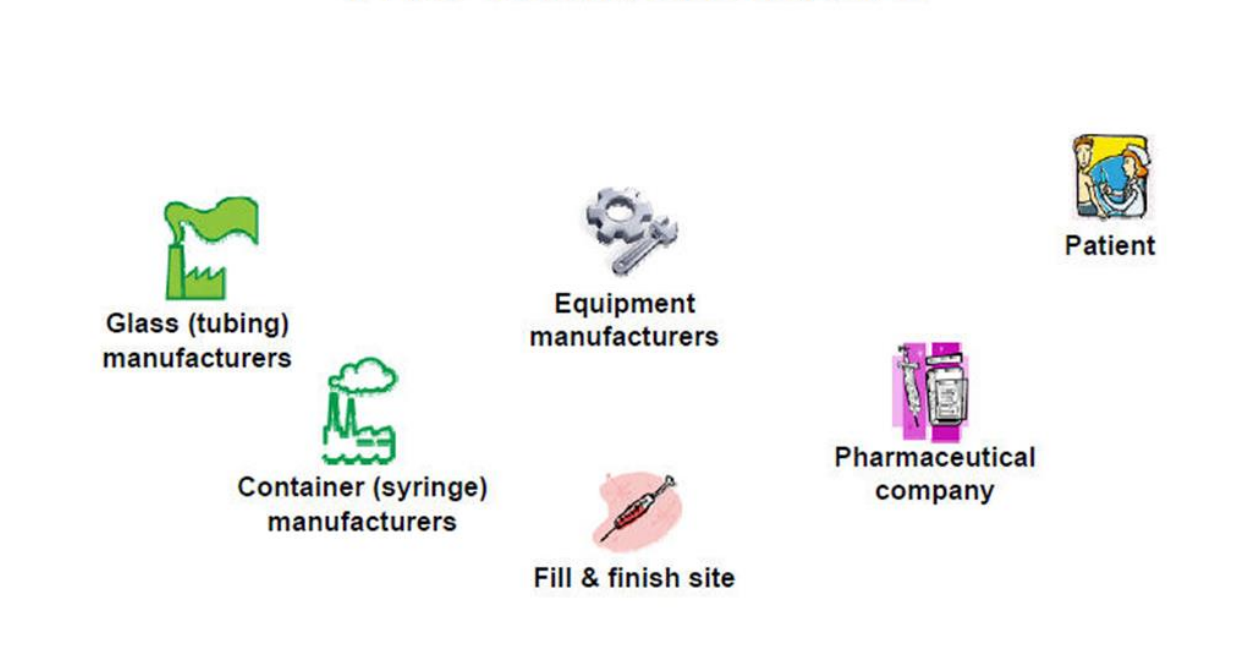
Machine Use of Glass Primary Packaging Material

Machine Runability



Machine Runability

The Stakeholders

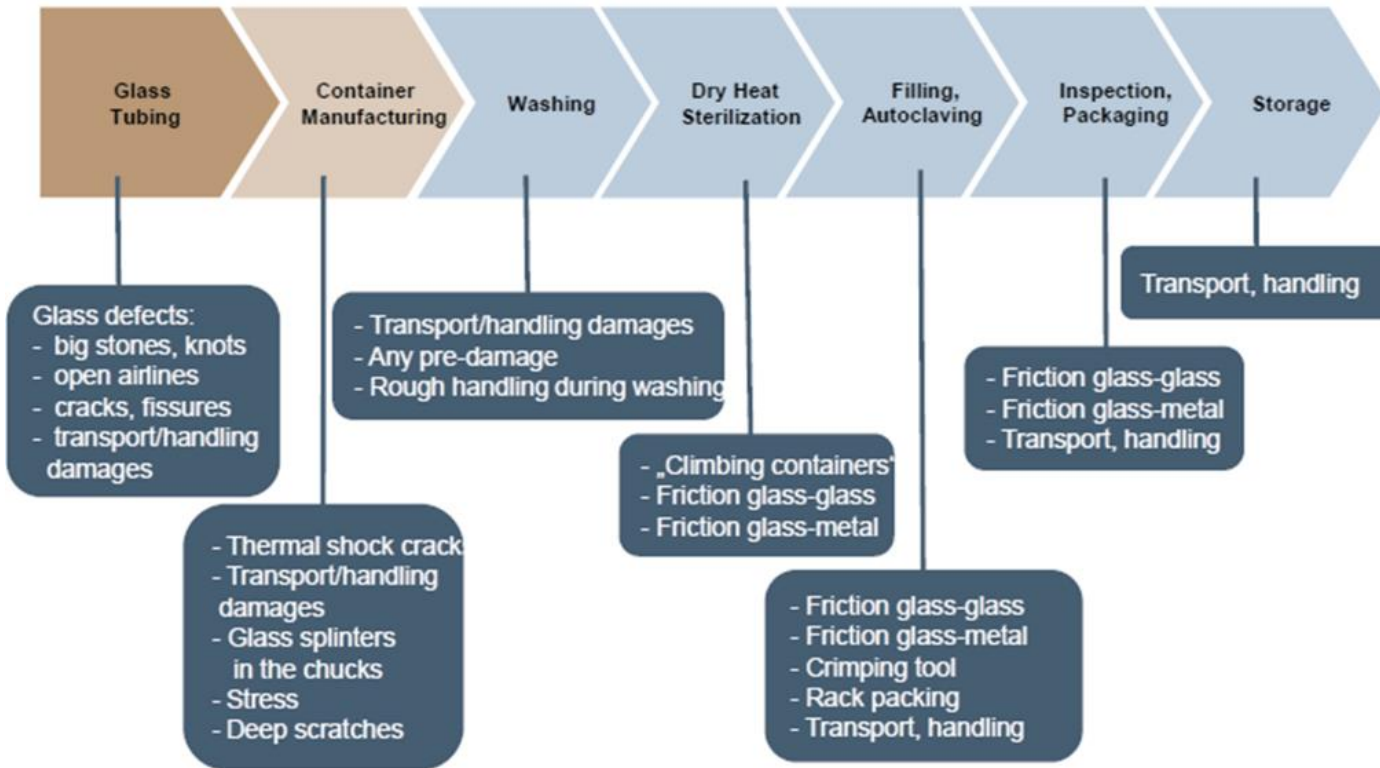


Dr. Andreas Rothmund, Vetter
PDA IG Meeting April 2010,
Zero Glass Breakage – Dogma or Ambitious Goal

Machine Runability

Breakage: Process Analysis

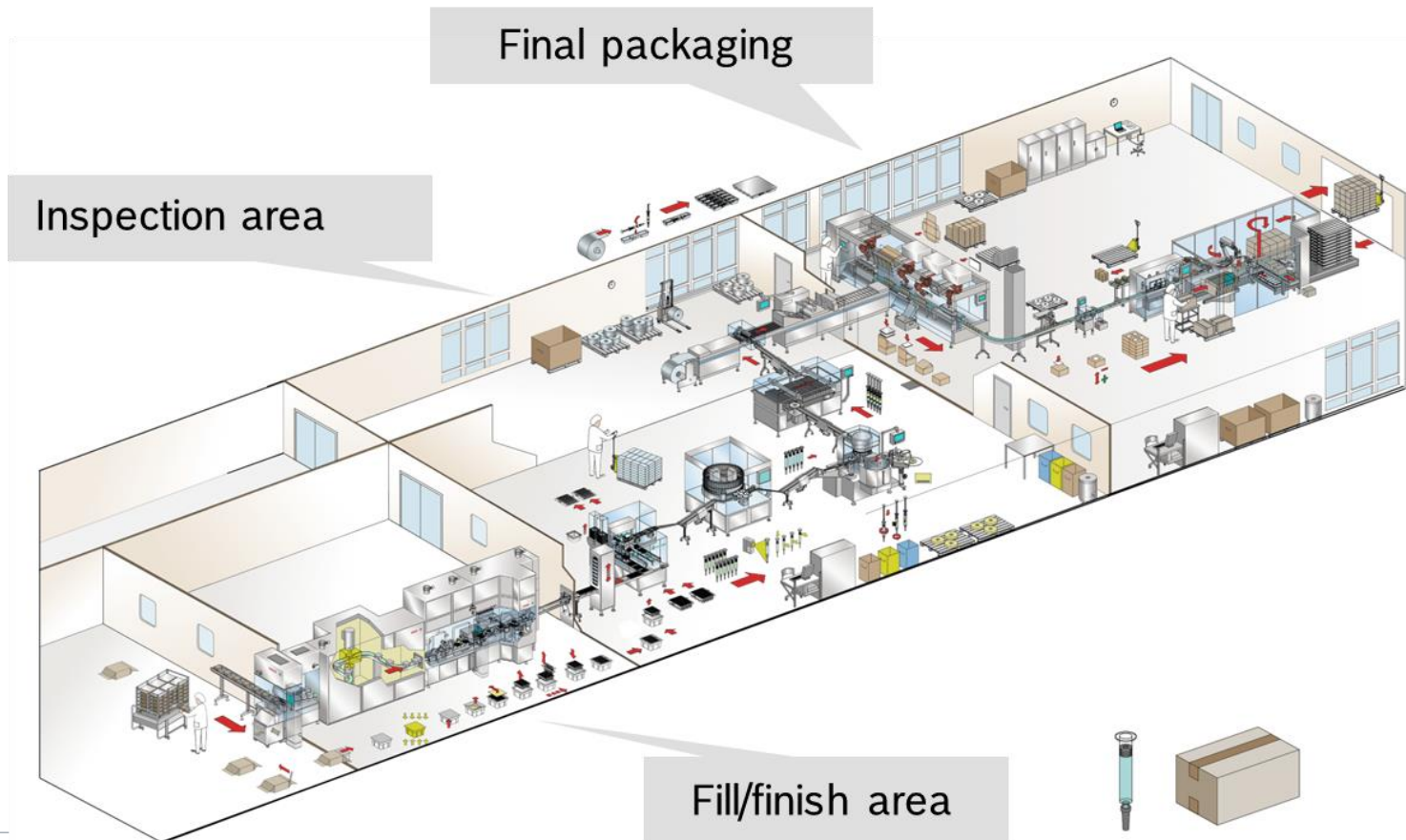
What can lead to breakage in the converting or filling process?



Source: Schott AG




Machine Runability

- The way of a syringe/cartridge



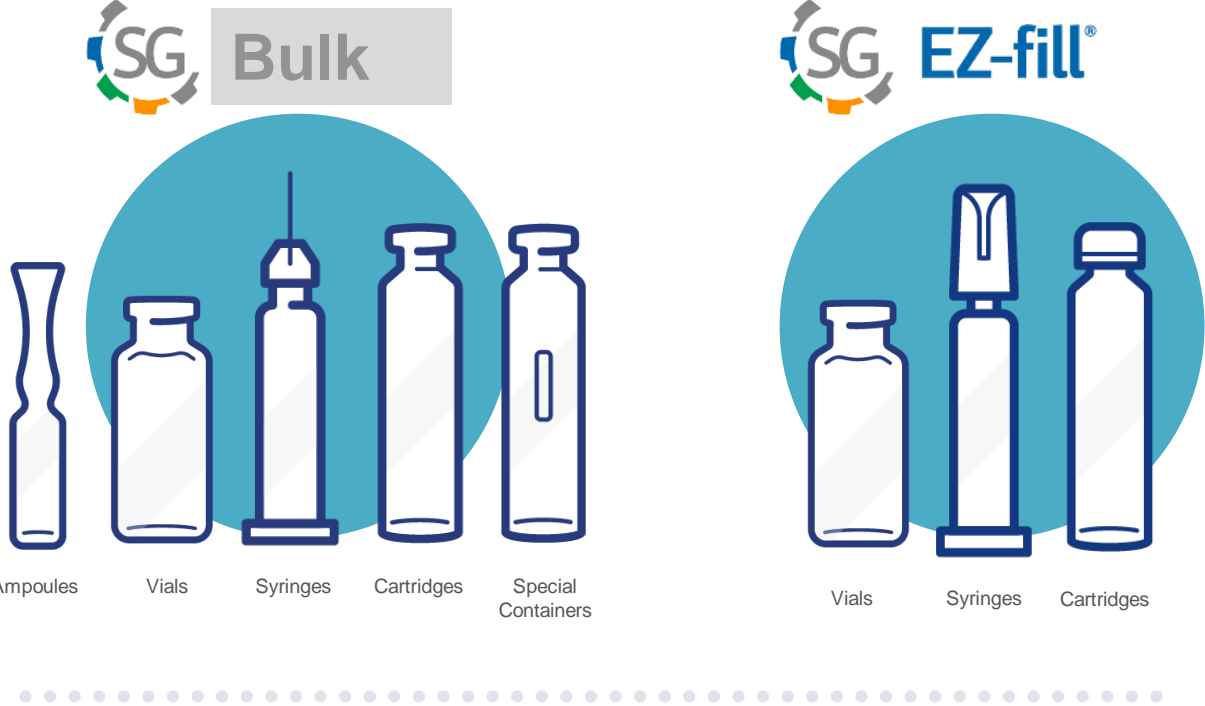
Machine Runability

- Comparison of glass types to be processed – example for vials

	 Tubular Glass	 Moulded Glass
Sizes (DIN EN ISO)	2R – 100R (DIN EN ISO 8362-/2016-06)	5H – 100H (DIN EN ISO 8362-4/2011-12)
Weight (g)	2R – 4,4g (Norm) 50R – 34,6g (Norm) 100R – 60g (Norm)	5H – 14g 50H – 50g 100H – 89g
Tolerances (mm)	2R ± 0,15 50R ± 0,4 100R ± 0,5	5H ± 0,4 50H ± 0,8 100H ± 0,8
Vial spec.: Blowback (to minimize risk of stopper pop up)	Yes - Difference between US and EU 	Blowback not possible due to production
RTU Availability for vials	Yes – 2R-50R (100R Option)	Yes – 20H-100H

Machine Runability

- Overview RTU vs. Bulk availability



Source: Stevanato Group

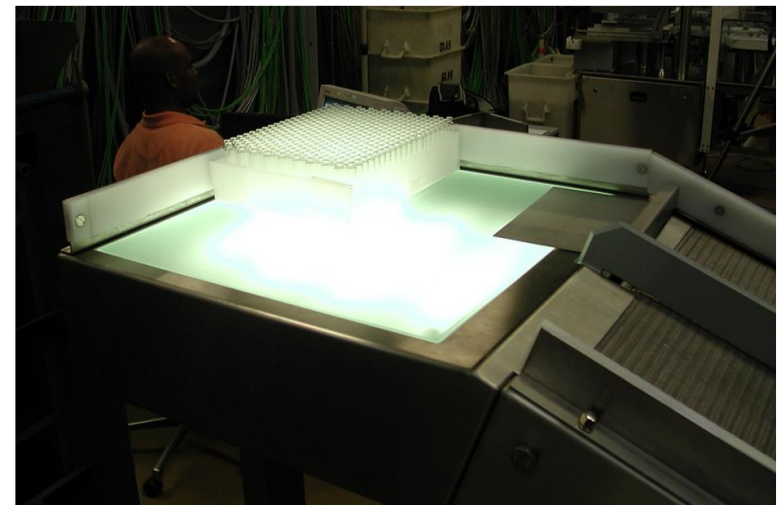
Machine Runability

- Glass quality

Practical Example: sampling & pre-inspection

Machine Runability

- It can be important to know and understand the characteristics of the container of individual suppliers and their forming lines
- Special “simple” solution for detecting glass breakage – beside customer defined sampling: “Light table in front of washing machine”

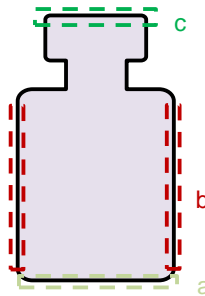


Machine Runability

- Empty vial inspection | Overview

Inspection areas

- Bottom inspection (a)
- Opening inspection (c)
- Sidewall inspection (b)



- Inspection of bottom + opening through vial opening (keyhole principal) with special optics each
- Inspection of sidewall with four cameras from the side
- Inspection for **particles** (e.g. splinters) and **glass defects** (e.g. scratches, cracks)
- Defect size $\geq 100\mu\text{m}$

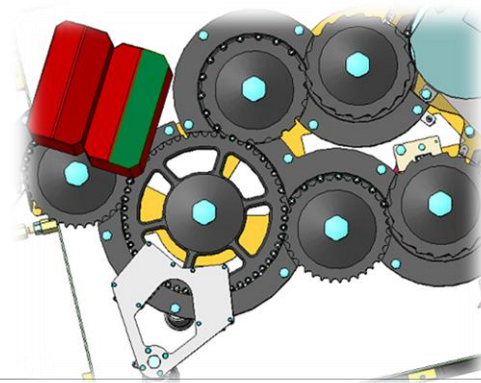
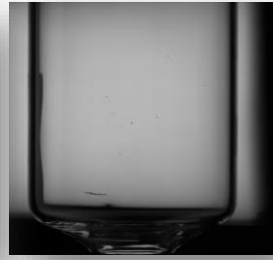
Bottom



Opening

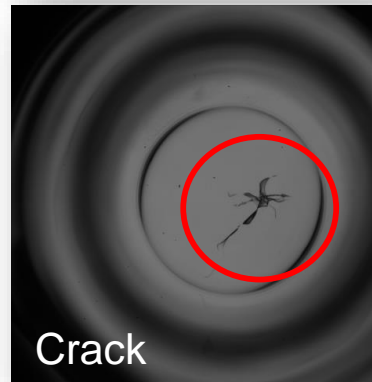
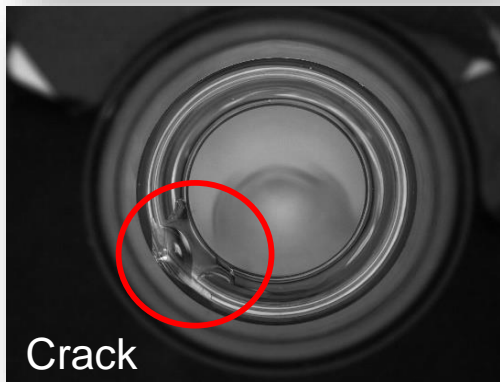
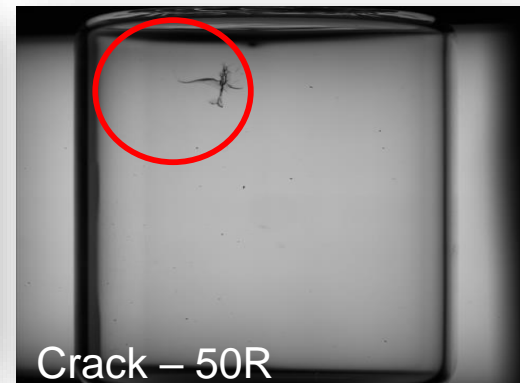
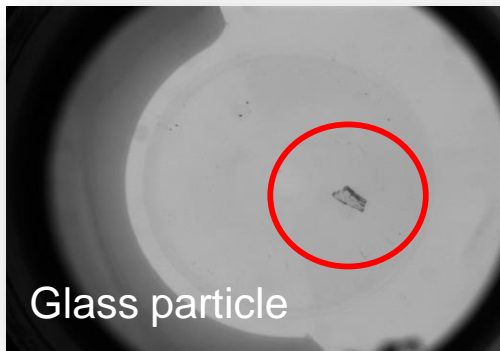


Sidewall



Machine Runability

- Empty vial inspection | Example images

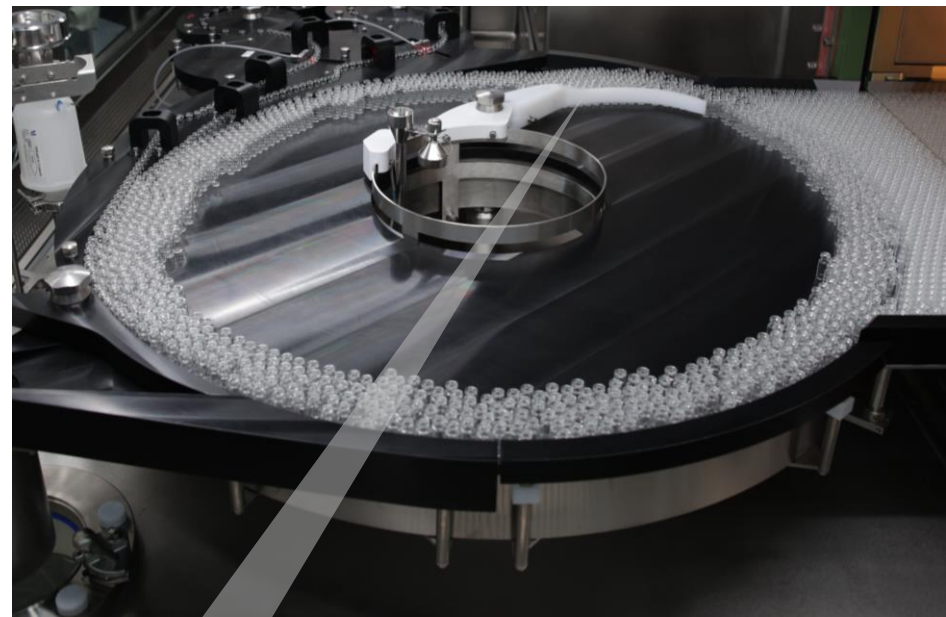
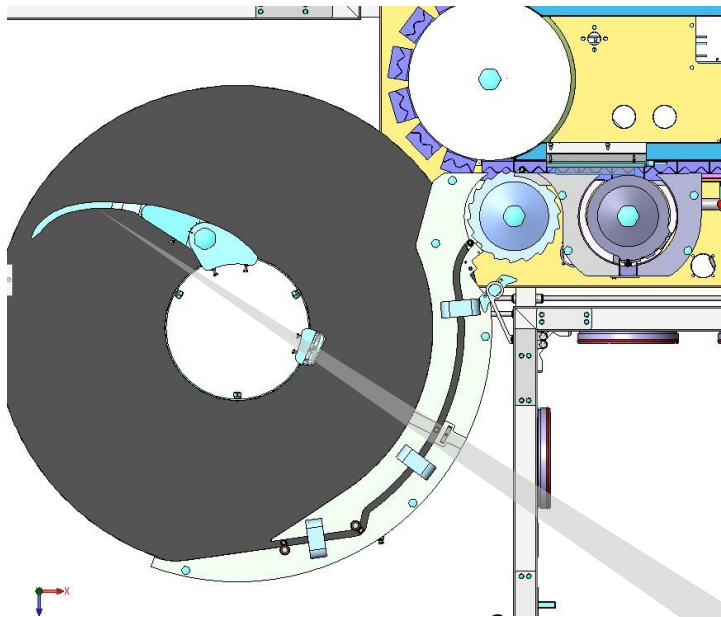


Machine Runability

- Roughness of containers
- Influence of tolerances & geometry
- Impact on machine speed

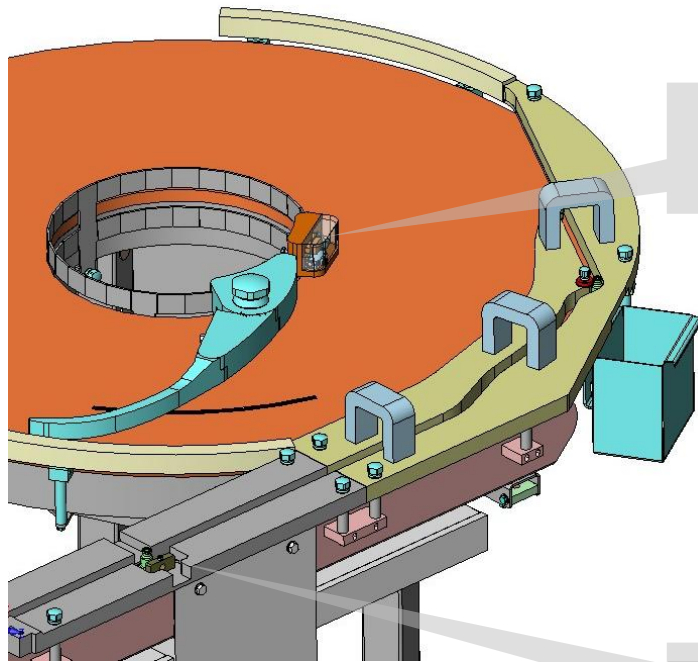
Practical Example: singularization of vials

Machine Runability

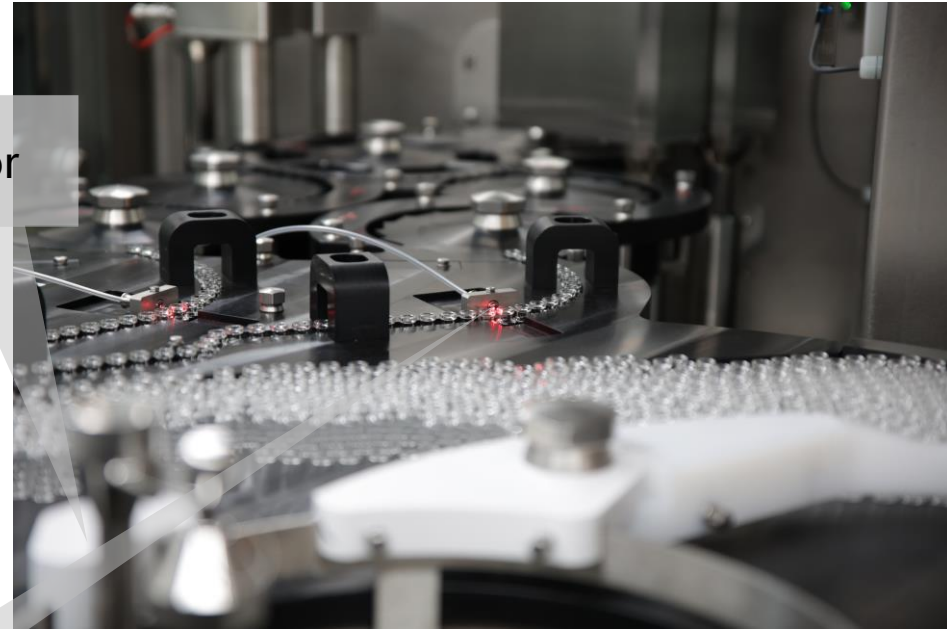


Flexible arm

Machine Runability

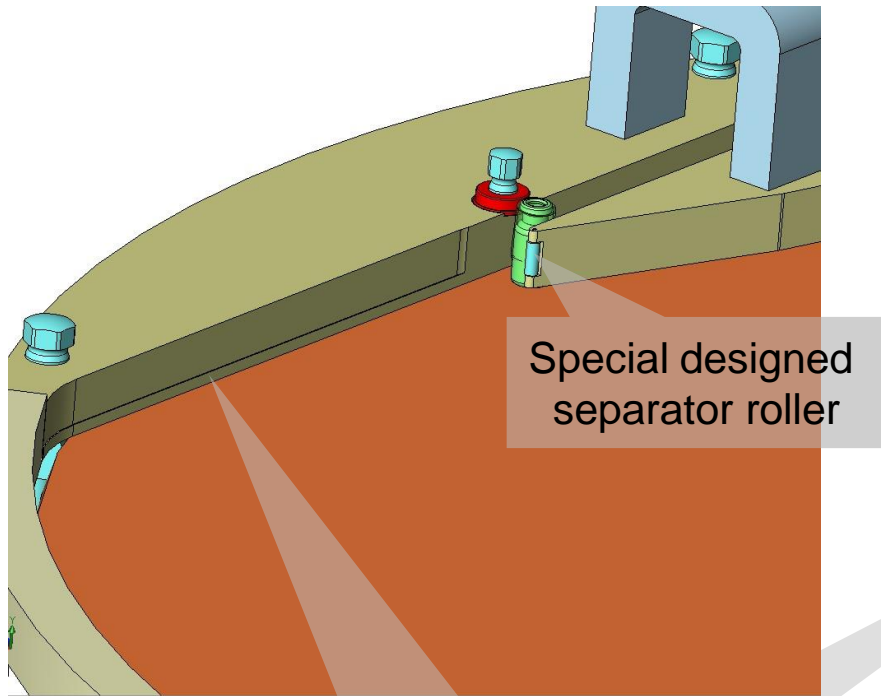


IR Sensor



MIN Sensor

Machine Runability

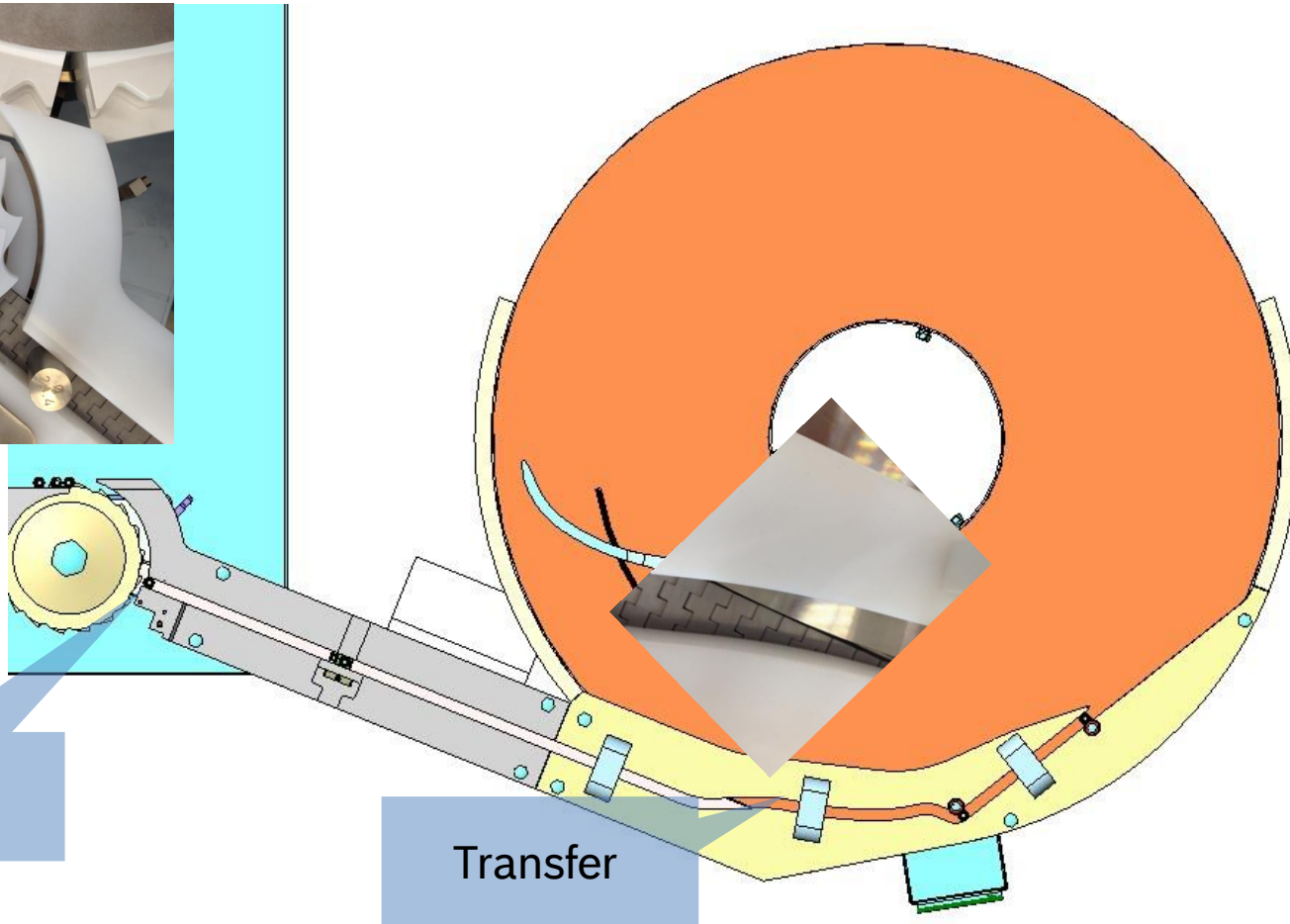


Special designed separator roller



Chamfer for small vials

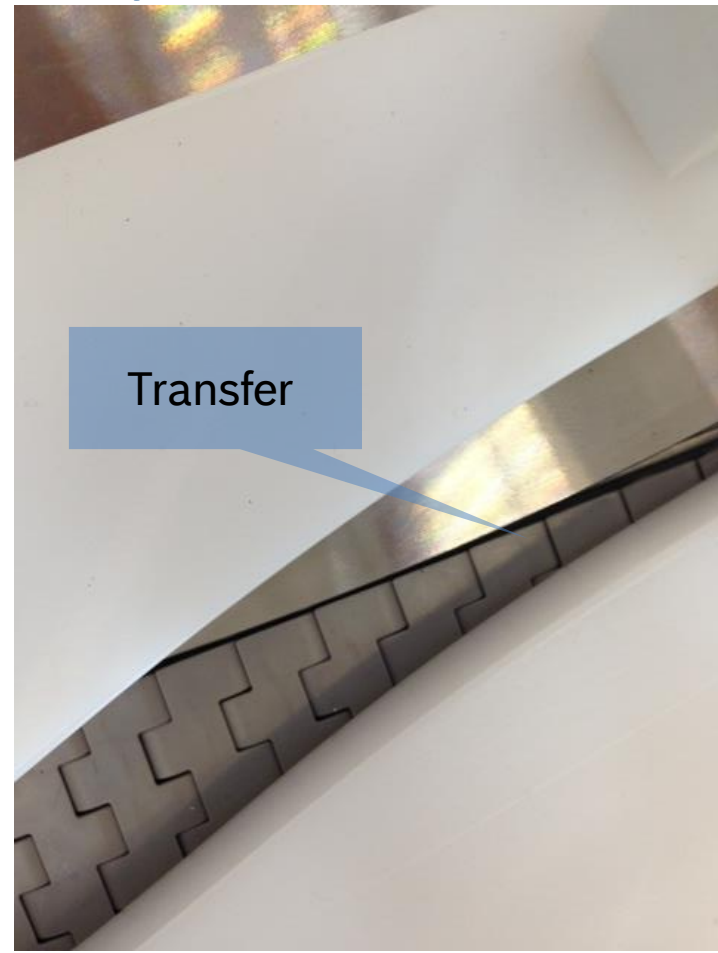
Machine Runability



Transfer

Transfer

Machine Runability



Machine Runability

- Tolerance of containers:
 - Design of size parts with play
- Roughness of containers :
 - Material composition and geometric adaption size parts:
 - Target: reduce friction

Machine Runability

- Improvements on turntable: Significant reduction of glass damage / breakage by using specially designed separator roller

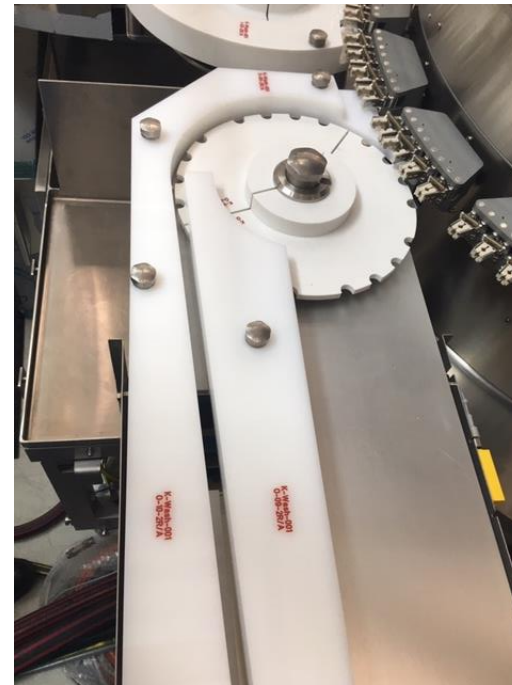


Separator
with roller



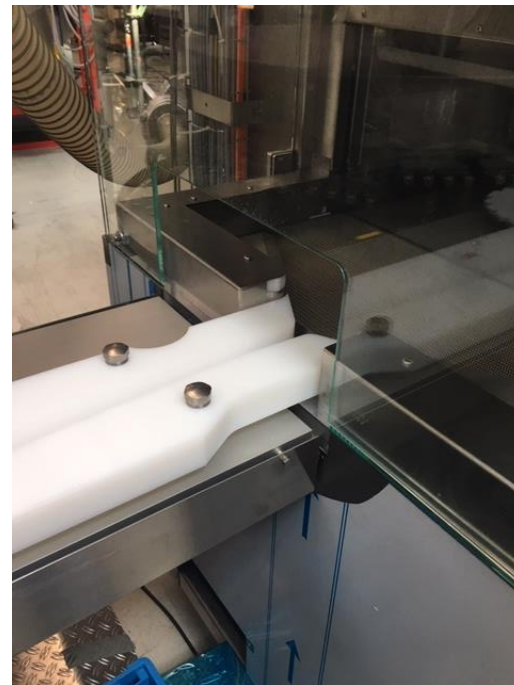
Machine Runability

- Improvements on transport to sterilizing tunnel: New material for format parts to reduce surface friction → Reduction of glass damage or breakage



Machine Runability

- Improvements on transport to sterilizing tunnel: New material for format parts to reduce surface friction → Reduction of glass damage or breakage



Machine Runability

- Tolerance of containers:
 - Design of size parts with play
- Roughness of containers :
 - Material composition and geometric adaption size parts:
 - Target: reduce friction
 - Outer Coating of containers :
 - Silicone
 - Special containers: Corning
 - Special coated containers: Schott, SG, Gerresheimer, Corning, ...*)
- Geometry of containers:
 - Single lane infeed vs. double lane infeed

* Only examples – listing not exhaustive

Machine Runability

- Single lane infeed vs. double lane infeed



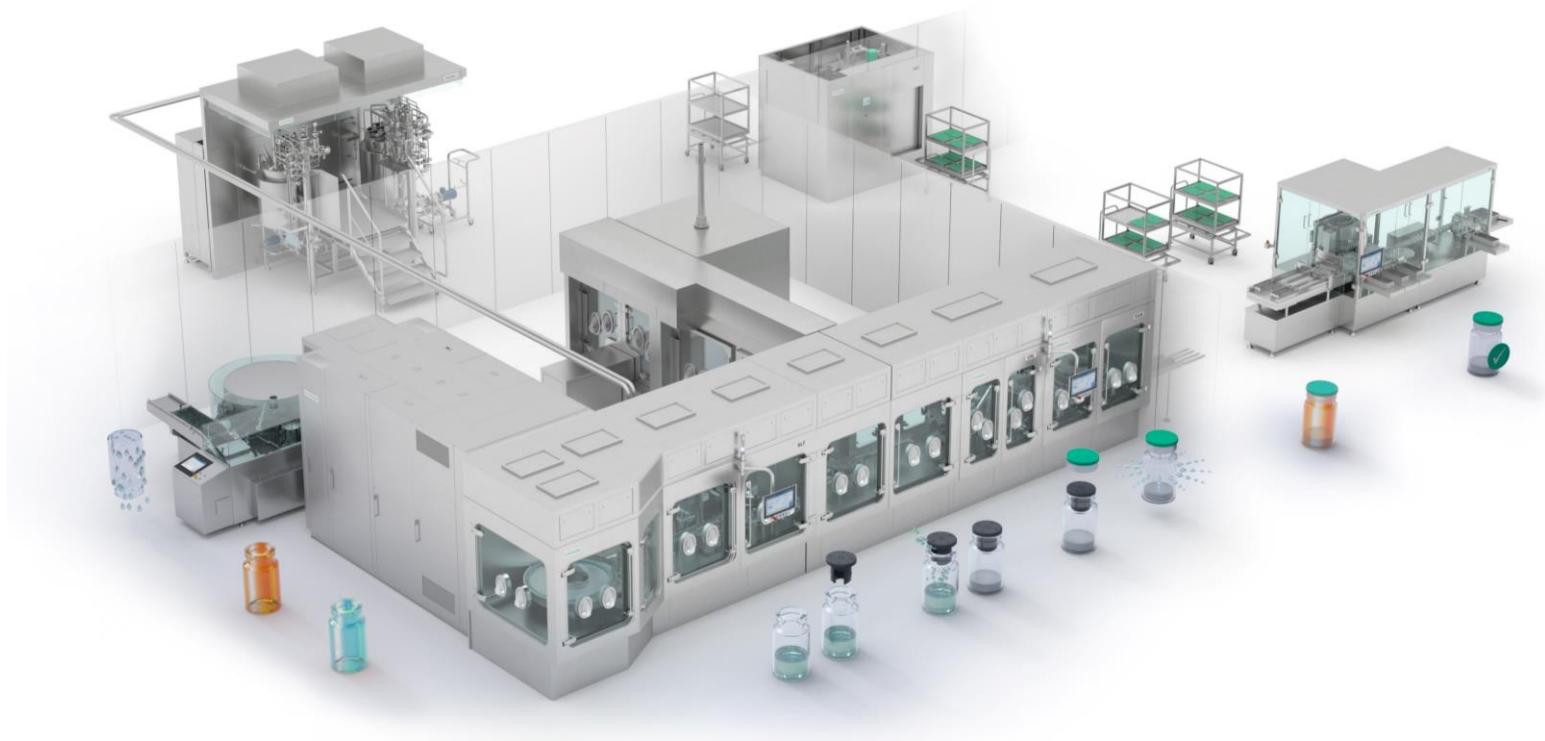
Machine Use of Glass Primary Packaging Material

Along the Process Chain – and where is impact on the glass ?



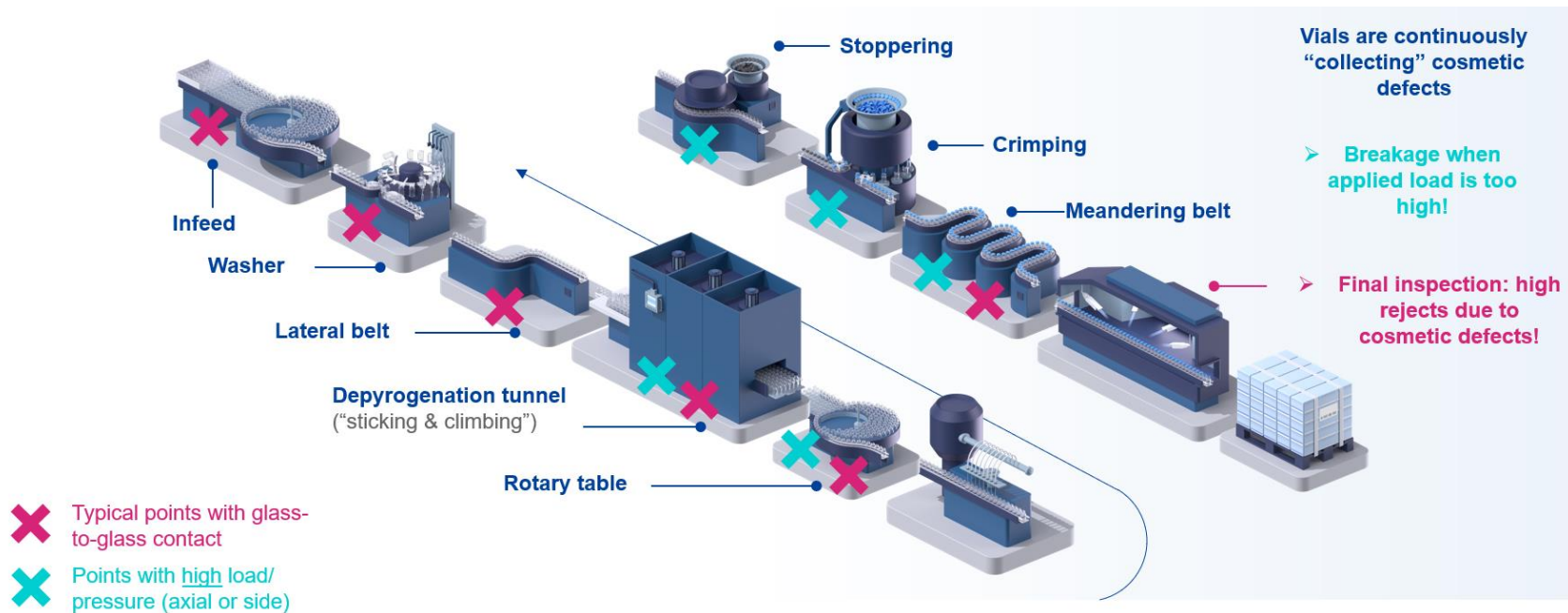
Along the Process Chain

- „The classical way of aseptic fill & finish“ - BULK



Along the Process Chain

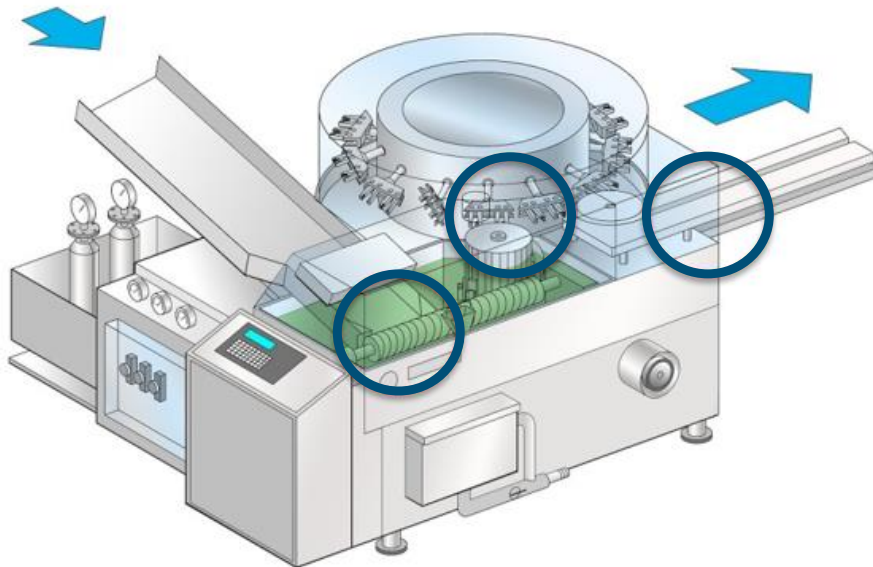
- Glass-to-glass contact + loads during bulk fill and finish
 - Vials experience glass-to-glass contact, side compression and axial pressure on various points



Source: SCHOTT AG

Along the Process Chain

- **First step: Cleaning**

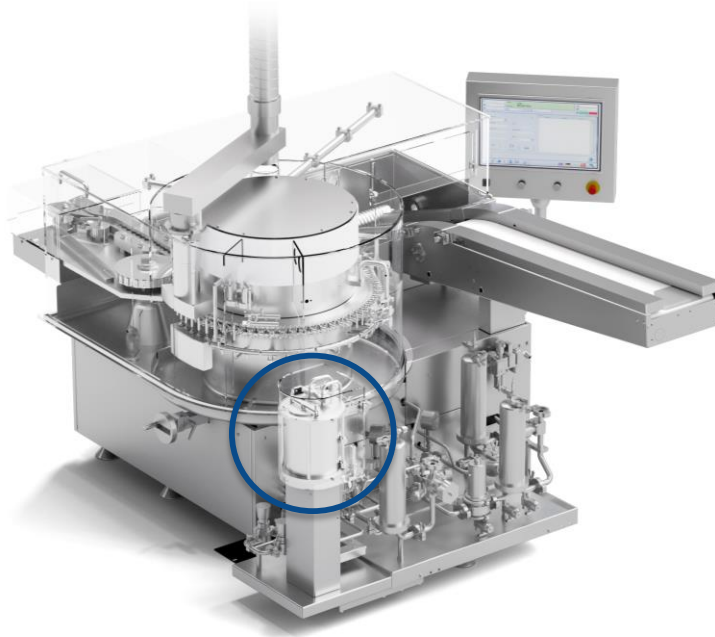


- **Critical areas – washing**

- Bulk infeed and singularization
- Needle for water and sterile air entering into containers several times
- Glass-to-glass contact at handover to sterilizing tunnel

Along the Process Chain

- **First optional step: Siliconizing**



- **Critical areas - siliconizing**

- Needle for water and silicone entering into containers several times
- Note:
 - Inner coating mainly for cartridges and syringes
 - Outer coating for vials and cartridges

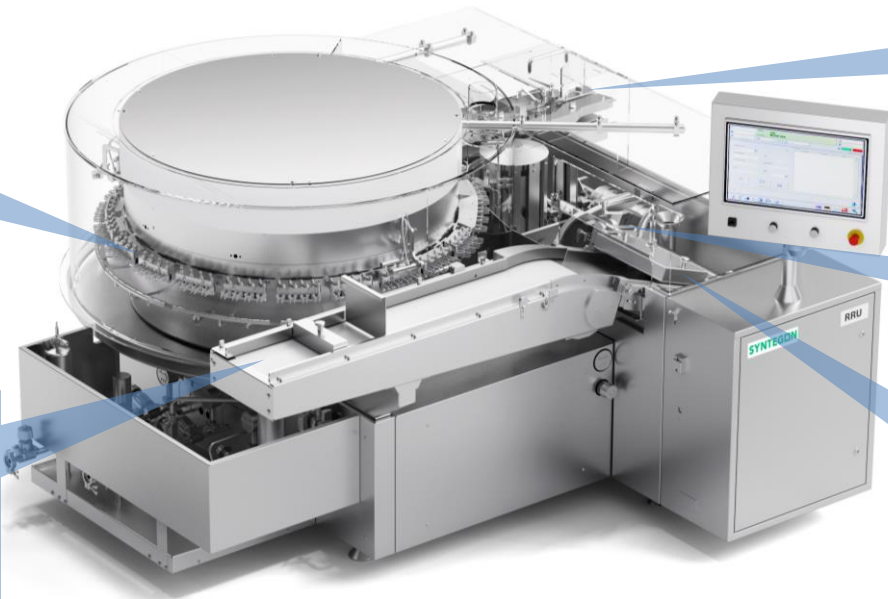
Along the Process Chain

- **First step: Cleaning**
Solutions for less stress on the glass



Servo ensure precise and reproducible needle movement

Infeed magazine on a belt conveyer – ensures safer separation especially for high output



Single lane feeding to tunnel

Scroll conveyer system incl. jam protection

Ultrasonic bath

Along the Process Chain

- Important transfer: Sterilization & Depyrogenation

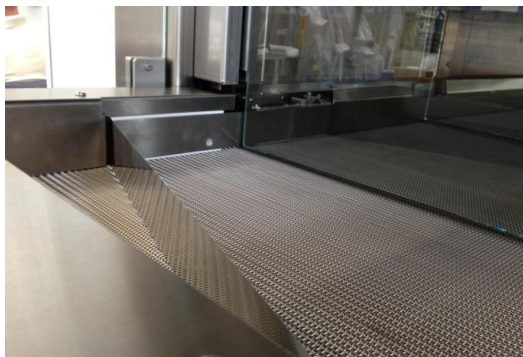


- Critical areas – Sterilization

- Direct glass-to-glass contact within the system
- Pressure on containers in tunnel infeed section
- Heating of glass containers up to >300 degrees Celsius
- Reduction/destruction of the water skin of the glass → sticky and scratch sensitive containers

Along the Process Chain

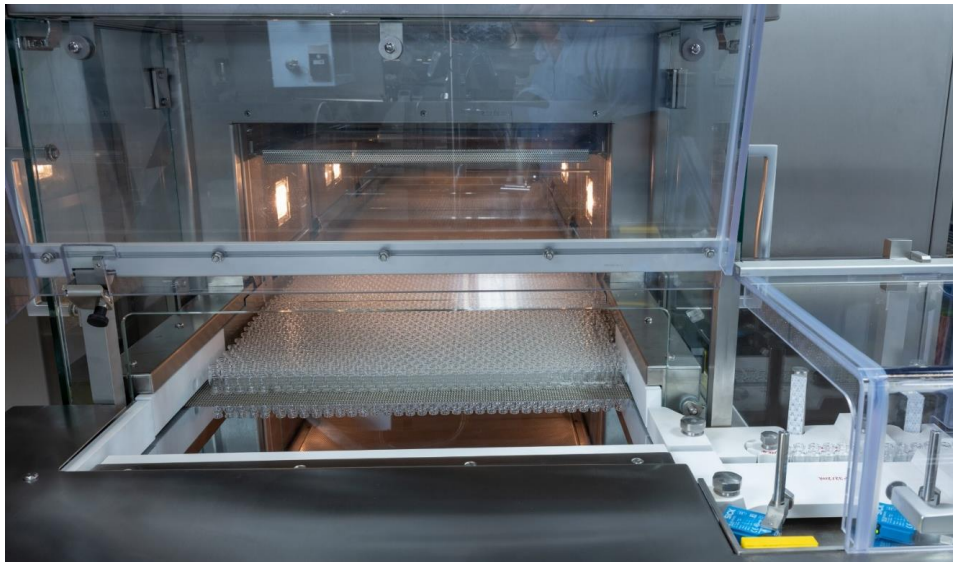
- **Important transfer: Sterilization & Depyrogenation**
Solutions for less stress on the glass



- Pre-Heating Zone to reduce temperature influence
- Automatic Density Control System
 - Output of cleaning machine adjusted according to tunnel load
- Usage of a 3 belt system
 - Friction-free, gentle container conveyance
 - Side belts moving synchronized together with main belt
 - Side belt design ensures reduced relative movement of containers due to even surface
- Transport width increases in sterilizing area to reduce stress to glass
- Row-by-row loading for hexagonal arrangement with minimal contact

Along the Process Chain

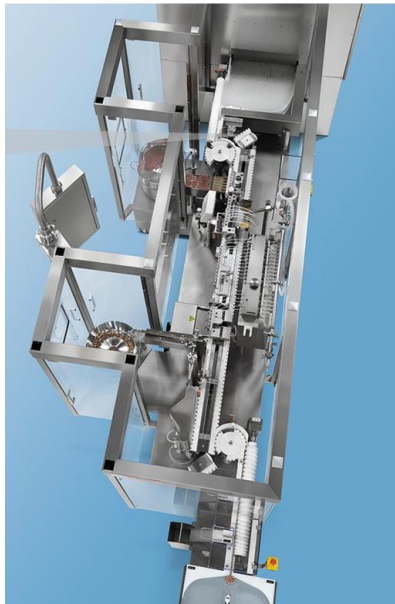
- **Important transfer: Sterilization & Depyrogenation**
Solutions for less stress on the glass



Row by Row –
Loading Zone

Along the Process Chain

- The core element: Filling & Closing

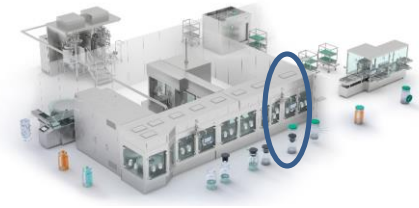


- Critical areas – filling & closing

- THE neuralgic point: separation of glass containers after sterilization
- Required precision for filling
 - example cartridges for pen systems:
 - Hole for filling inner- \varnothing $3,15 \pm 0,2$ mm
 - Filling needle outer- \varnothing 2 mm
 - = only 0,5 mm air gap!

Along the Process Chain

- Seal the deal: Capping



- Critical areas – capping

- Wide tolerance range of diameter of neck can cause problems at cap pick up
- Possible uneven bottom surfaces can cause bad crimping results
- Not completely round containers sway - bad crimping results



Along the Process Chain

- **The core element: Filling & Closing + final Capping**
Solutions for less stress on the glass



Filling carrier system:

- Precise and individual transportation through the filling and closing machine
- Additional centering station where needed

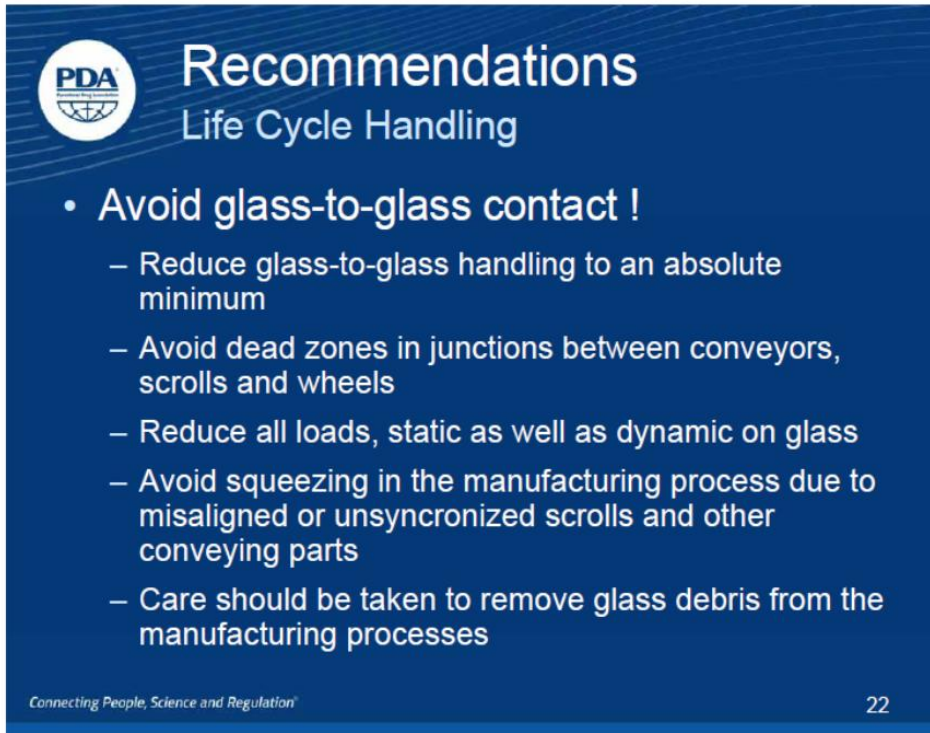
Closing station:


- Adjustable and controlled pressure (buffer systems to adjust tolerances)
- Cartridge is rotated from both ends
- Spring loaded rollers to accomplish tolerances



Along the Process Chain

- How can the impact be reduced in general?



 **Recommendations**
Life Cycle Handling

- **Avoid glass-to-glass contact !**
 - Reduce glass-to-glass handling to an absolute minimum
 - Avoid dead zones in junctions between conveyors, scrolls and wheels
 - Reduce all loads, static as well as dynamic on glass
 - Avoid squeezing in the manufacturing process due to misaligned or unsynchronized scrolls and other conveying parts
 - Care should be taken to remove glass debris from the manufacturing processes

Connecting People, Science and Regulation® 22

Mads Reedtz Espersen,
Novo Nordisk
PDA Parenteral Meeting,
October 2010,
Supply Chain Issues -
Glass breakage from
Purchase
to Dispatch

Machine Use of Glass Primary Packaging Material

What to Consider, What are Common Problems, How to Avoid Them



Problems and solutions

- **Three major ways to improve glass handling**
 - 1) Improve classical bulk fill & finish processes
 - 2) Bulk Fill & finish process with no glass-to-glass transport
 - 3) Ready-to-use process (tub/nest or tray)

Problems and solutions

- **1) Improve classical bulk fill & finish processes**
 - Optimized machine design
 - Various options for buffering and transfers
 - Machine Simulations
 - Cooperation with partners as f. ex. packaging suppliers, vision experts,...

Problems and solutions

- 2) Bulk Fill & finish process with no glass-to-glass transport



Problems and solutions

- Robotic feeding



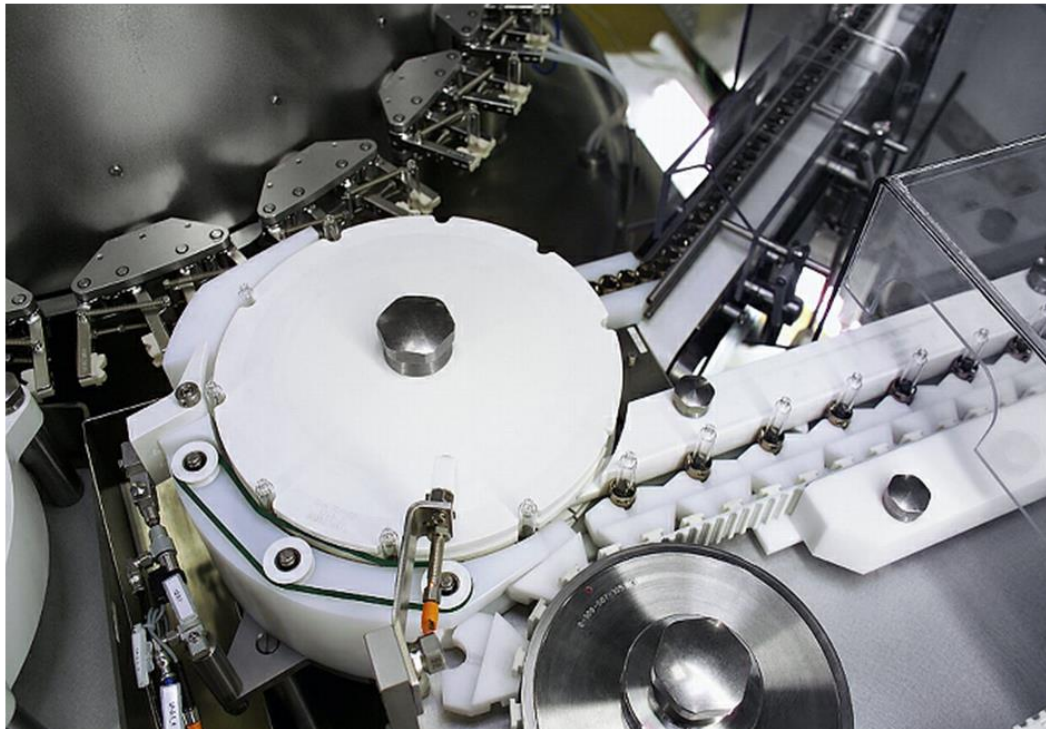
Problems and solutions

- Stainless steel transport pucks



Problems and solutions

- Washer outfeed/tunnel infeed - detail



Problems and solutions

- Infeed filling machine with transport pucks



Special transport carriers



Problems and solutions

- Infeed with robotic systems and transport tray



Problems and solutions

- Infeed with robotic systems and transport tray



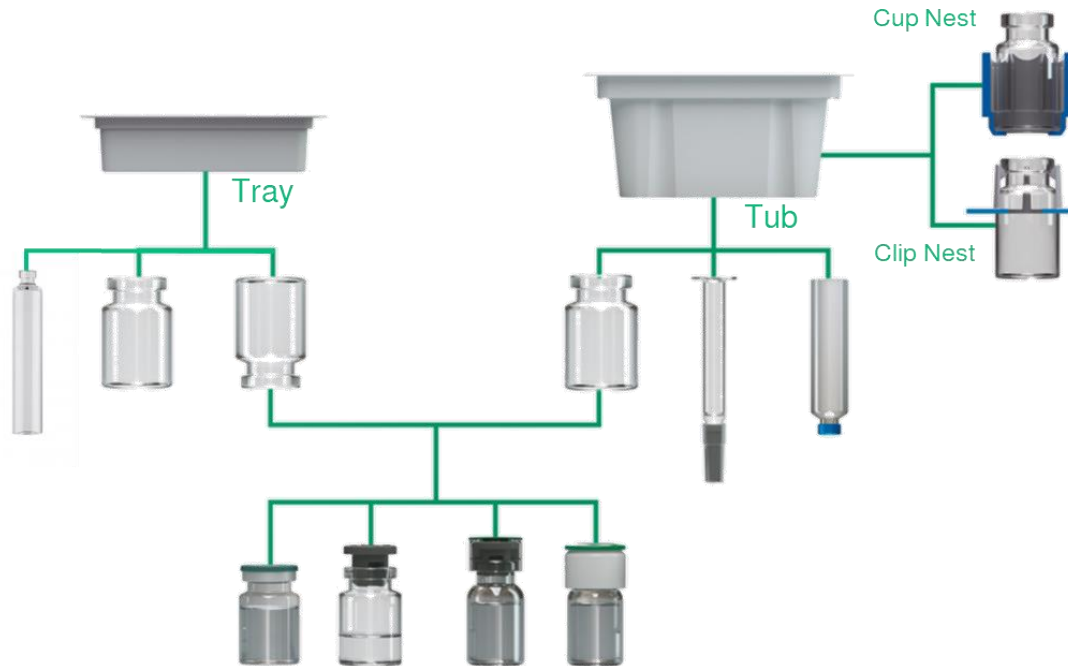
Problems and solutions

- Infeed filling machine with transport pucks



Problems and solutions

- 3) Ready-to-use process (tub/nest or tray)



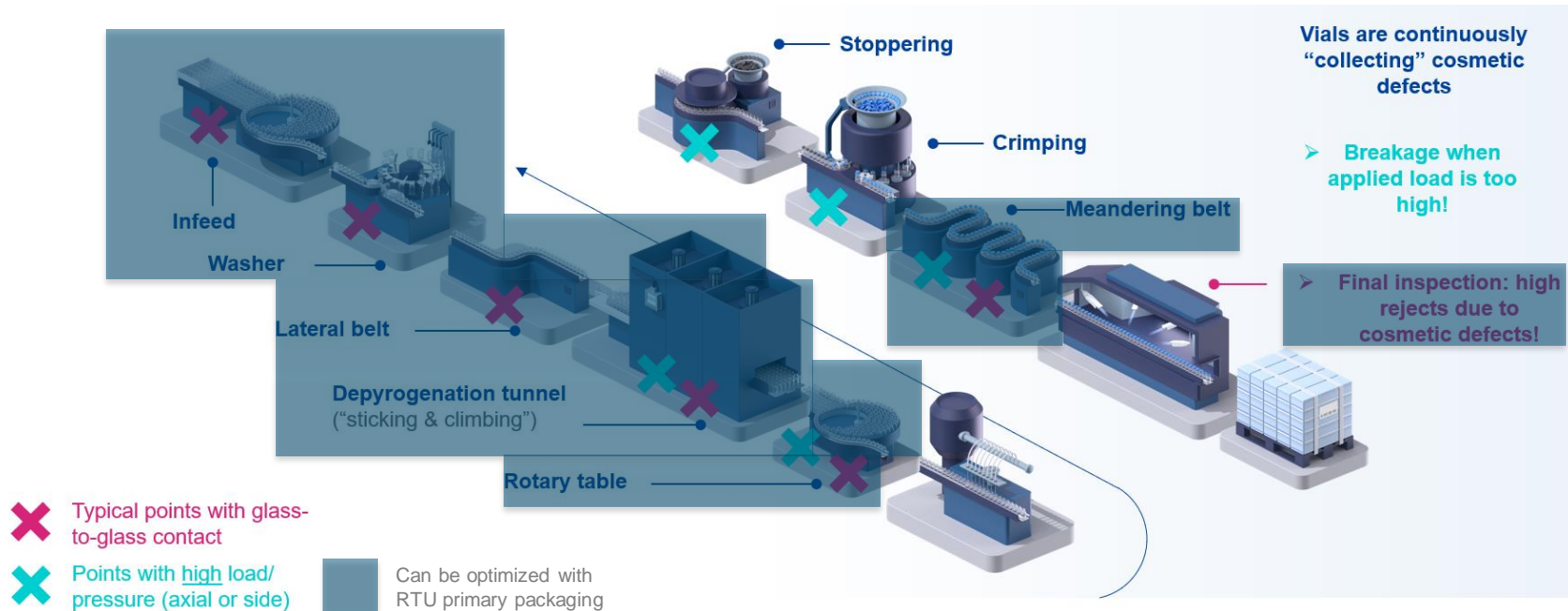
NO glass-to-glass contact - secondary packaging should preserve:

- cosmetic (f. ex. scratches)
- mechanical (f. ex. breakage)
- microbiological (f. ex. particles)

properties

Problems and solutions

- Glass-to-glass contact + loads during bulk fill and finish – compared to RTU process
 - Vials experience glass-to-glass contact, side compression and axial pressure on various points



Source: SCHOTT AG

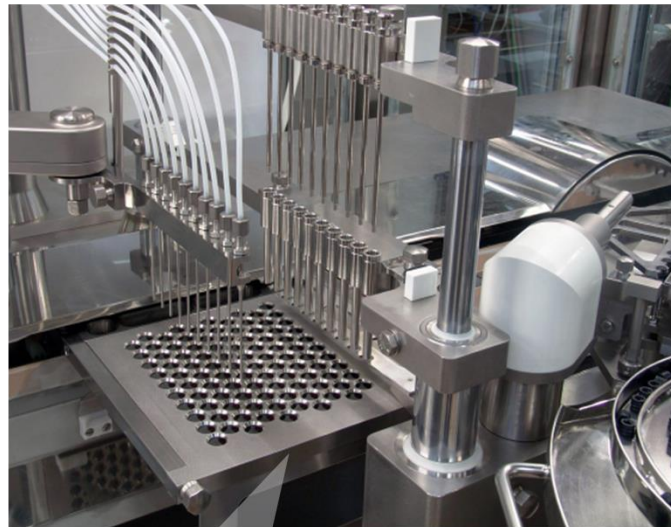
Problems and solutions

- Example: tub/nest processing for syringes

Nested syringes



filling &
closing



Centering plate
stainless steel



Problems and solutions

- Example: tub/nest processing for syringes

Nested syringes – alternative centering plate



filling &
closing

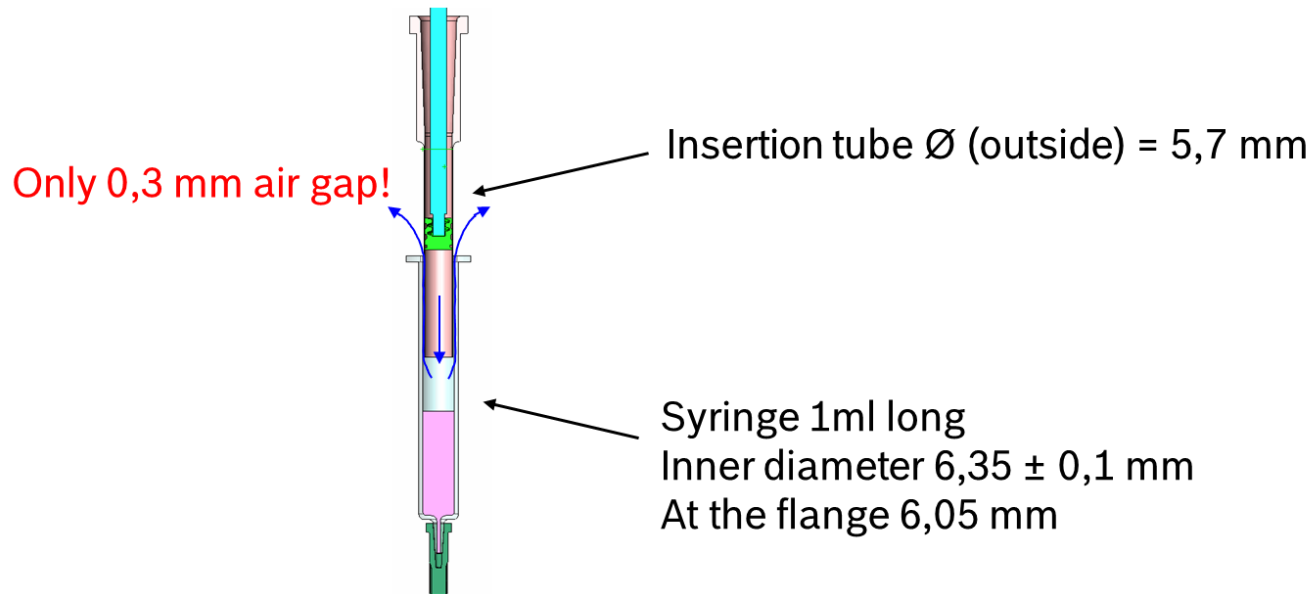
Centering plate
plastic material



Problems and solutions

- Example: tub/nest processing for syringes

Precision – Stoppering of syringes



Problems and solutions

- Example: tub/nest processing for syringes



Insertion tubes

Filling needles

Problems and solutions

- Example: tub/nest processing for vials



Problems and solutions

- Example downstream syringe: rod insertion and labeling



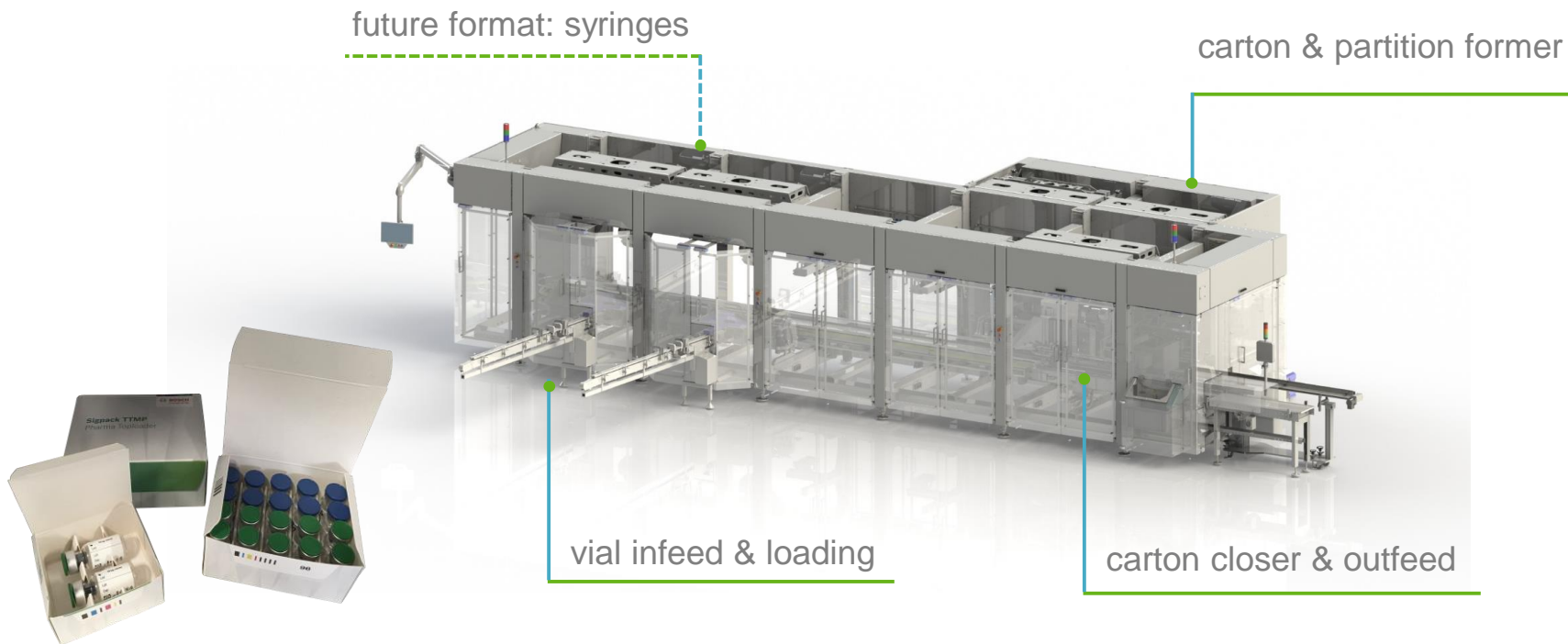
Problems and solutions

- Example downstream syringe: inspection



Problems and solutions

- Example downstream syringe/vial: top loader



Problems and solutions

- Alternative: robotic handling for fill & finish tasks



Machine Use of Glass Primary Packaging Material

Coordination Process Primary Packaging Material and Machine



Coordination & Cooperation

- Cooperation is key



Source: Depositphotos

Coordination & Cooperation

- Norms – hard to unite BUT they help in collaboration

	DIN ISO 11040-4	DIN
<p>ICS 11.040.25 Ersatz für DIN ISO 11040-4:2007-10</p> <p>Vorgefüllte Spritzen – Teil 4: Spritzenzylinder aus Glas für Injektionspräparate und sterilisierte und vormontierte Spritzen zur Abfüllung (ISO 11040-4:2015)</p> <p>Prefilled syringes – Part 4: Glass barrels for injectables and sterilized subassembled syringes ready for filling (ISO 11040-4:2015)</p> <p>Seringues préremplies – Partie 4: Cylindres en verre pour produits injectables et seringues pré-assemblées stérilisées préremplissables (ISO 11040-4:2015)</p>		

INTERNATIONAL STANDARD **ISO 21881**

First edition
2019-10

Sterile packaged ready for filling glass cartridges

Cartouches en verre préremplissables sous emballage stérile

INTERNATIONAL STANDARD **ISO 11040-7**

First edition
2015-04-01

**Prefilled syringes —
Part 7:
Packaging systems for sterilized
subassembled syringes ready for filling**

INTERNATIONAL STANDARD **ISO 21882**

First edition
2019-10

Sterile packaged ready for filling glass vials

Flacons en verre préremplissables sous emballage stérile

INTERNATIONAL STANDARD **ISO 11040-6**

Second edition
2019-01

**Prefilled syringes —
Part 6:
Plastic barrels for injectables and
sterilized subassembled syringes
ready for filling**

Coordination & Cooperation

- Example 1) Cooperation in design of new packaging materials

Example: Common machine test:

- Vial line (speed washer-tunnel-filler 500 vials per minute, speed capper 600 vials per minute) for 2R vials \varnothing 16 +/- 0,15 mm
- Tested vials:
 - **Valor vials:** \varnothing 16,75 mm +/- 0,25 mm
 - **Coated Borosilicate vials:** \varnothing 16,5 mm +/- 0,2 mm
 - **Borosilicate vials:** \varnothing 16,5 mm +/- 0,2 mm
- General setup of size parts: mechanical play 0,5 -1 mm

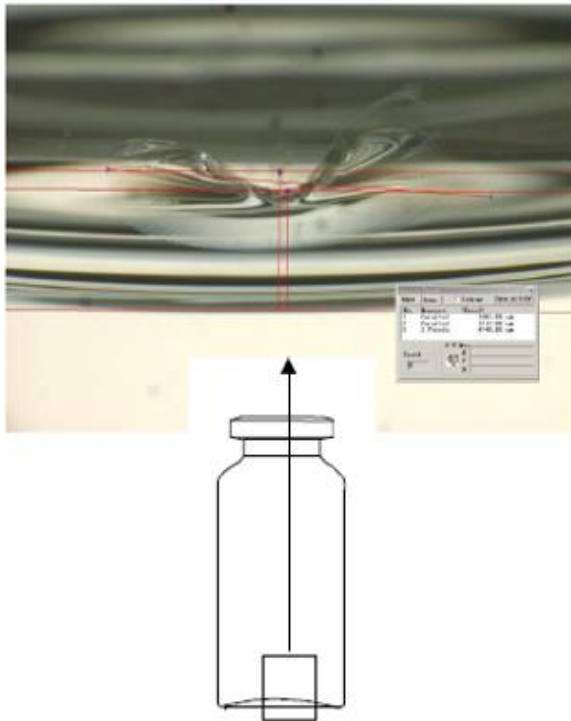
- Result:

- The classical borosilicate glass was not able to run on the line
- Outer coating can reduce glass defects, breakages, particles,...
- But can also help to overcome mechanical misalignments + achieve higher line speeds



Coordination & Cooperation

- Example 2) Common route cause analysis in case of failures
 - Case study at customer: vials damaged in bottom area



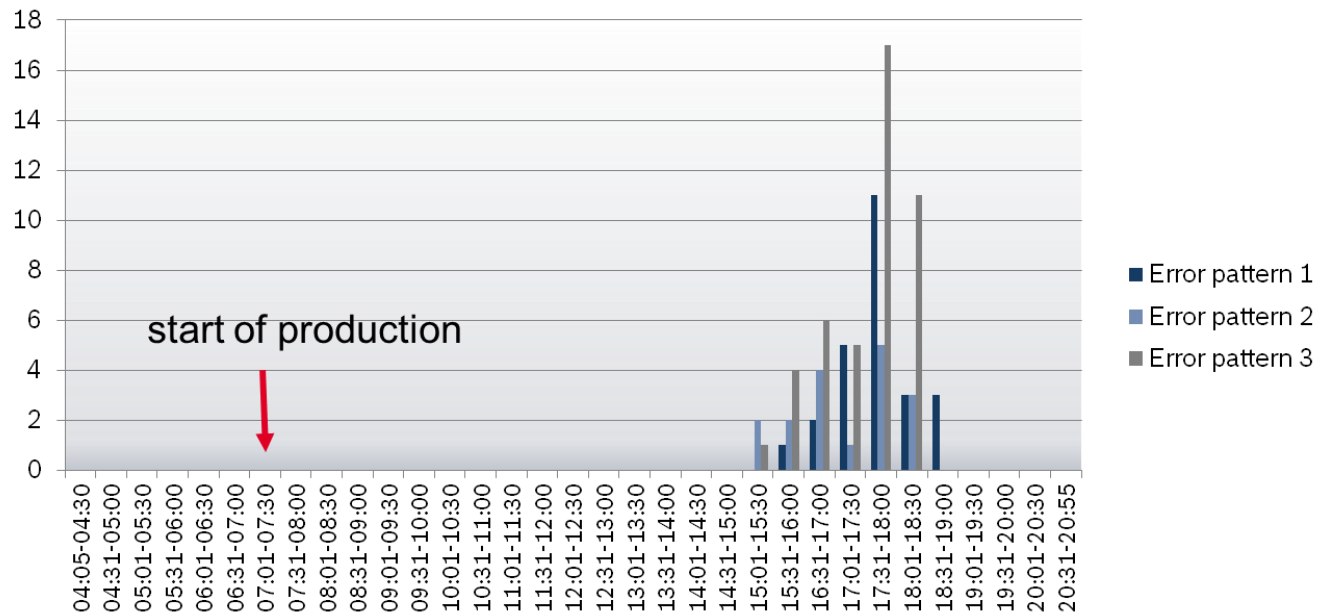
- Analysis by the customer

- Analysis with microscope
- Determination of the height of impact
 - Between 1,5 and 3,6 mm from bottom
- Three kind of different damages recognized

Coordination & Cooperation

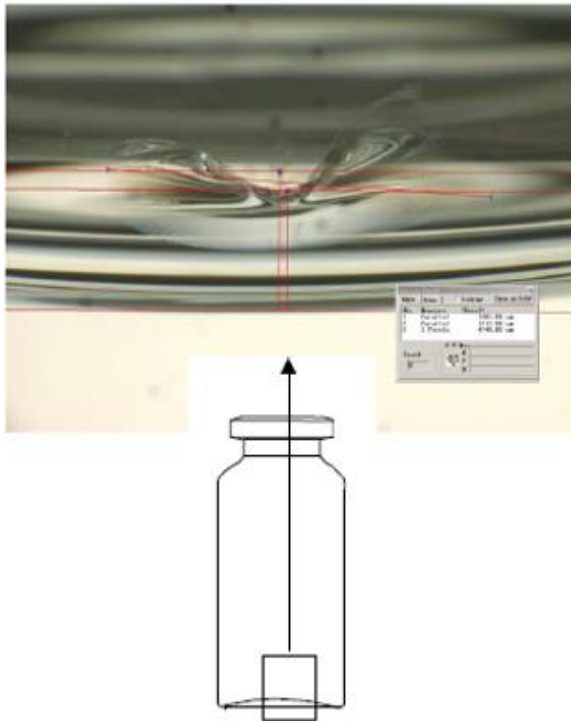
- Example 2) Common route cause analysis in case of failures
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Number of damages over time



Coordination & Cooperation

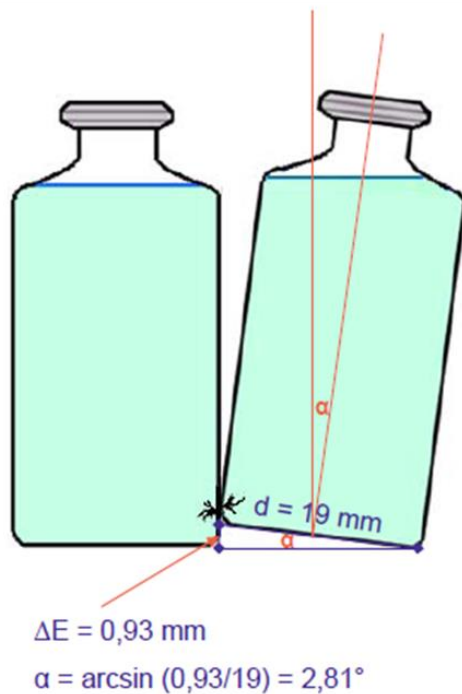
- Example 2) Common route cause analysis in case of failures
 - Case study at customer: vials damaged in bottom area



- Analysis by the glass manufacturer
 - Vials with all three kind of damages
 - Damages caused by glass to glass contact. No other materials found by analytical methods
 - Probably all damages have the same origin

Coordination & Cooperation

- Example 2) Common route cause analysis in case of failures
 - Case study at customer: vials damaged in bottom area



- Analysis by the glass manufacturer

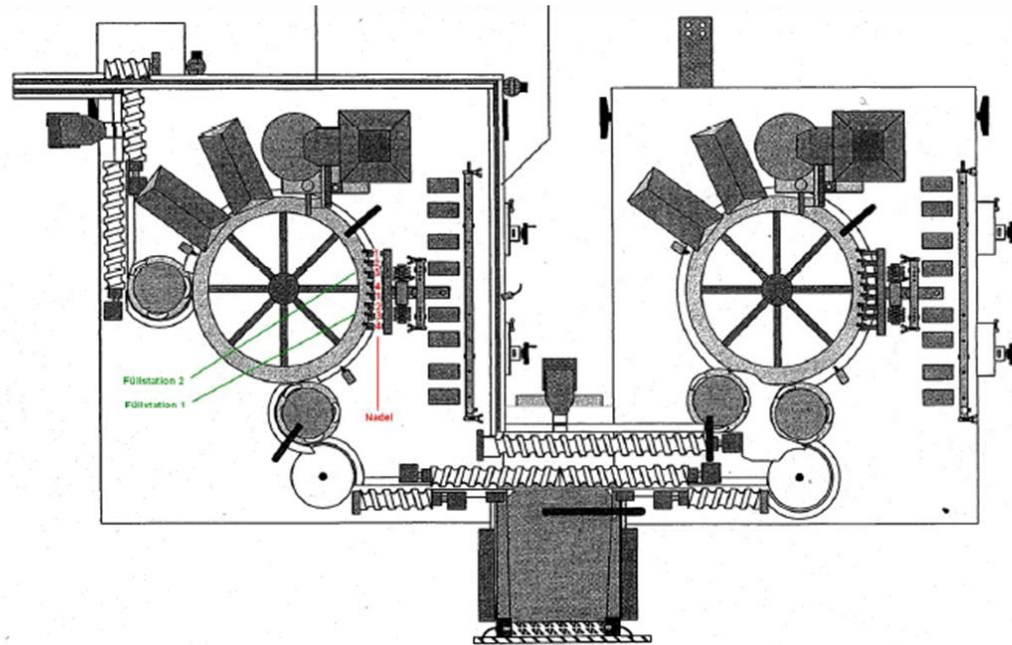
Crash constellation

Coordination & Cooperation

- Example 2) Common route cause analysis in case of failures
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Machine layout

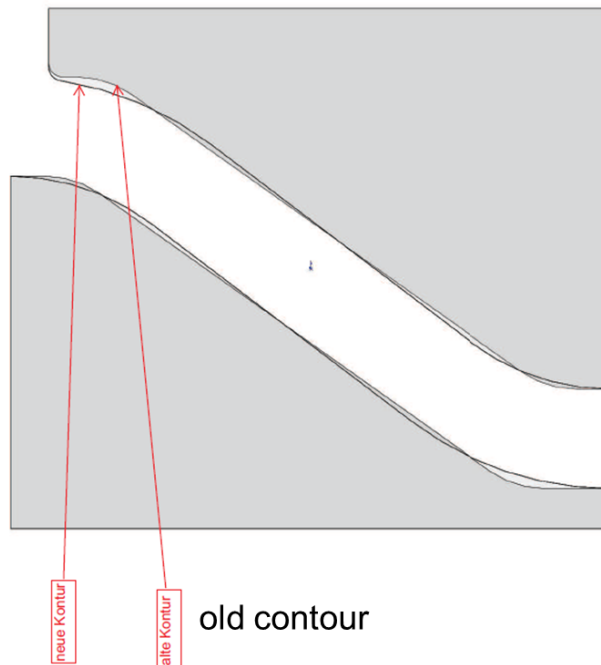
Critical spot:
Scroll onto a
belt



Coordination & Cooperation

- Example 2) Common route cause analysis in case of failures
 - Case study at customer: vials damaged in bottom area

New sizepart at outfeed



Small change → huge effect

new contour


old contour

Coordination & Cooperation

- Example 3) Inline measuring of pressure during bulk filling

Smart Skin Quantifeel™ Sensor Technology

Easy to interpret visualization for control of line setup and guidance to optimization



Sensor Drones

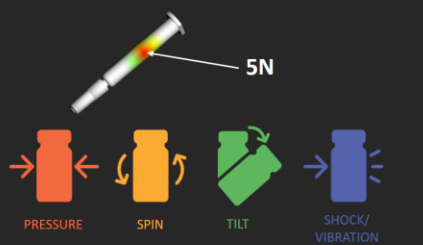
- ... pass lines just as the other containers to record position and time resolved forces

Quantifeel™ Software

- ... visualizes zones of high force onto processed containers

Pressure Measurement

Pressure maps show locations on drone skin and color indications of safe (green) to high pressure (red).

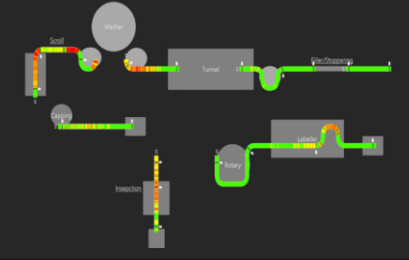


LIVE DATA ABOUT WHAT IS HAPPENING TO YOUR CONTAINER

- Pressure Measurement**
Our patented solution measures line pressure forces in high resolution which is critical to identifying specific causes of damage on the line.
- Line Mapping**
We present our data in a visual format that decision-makers can understand.
- Video Capture**
Simultaneous video capture enables precise review of the cause of damaging forces.

Line Mapping


Line Mapping Aggregates and Summarizes the Data to Look for Trends



- Pressure Measurement**
Our patented solution measures line pressure forces in high resolution which is critical to identifying specific causes of damage on the line.
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Simultaneous video capture enables precise review of the cause of damaging forces.

Live Video Capture & Data Sync

Data streams to tablet via Bluetooth and syncs with video feed for analysis and playback



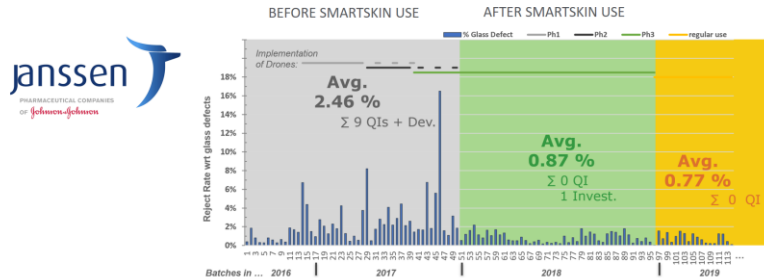
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Source: Smart Skin Technologies

Coordination & Cooperation

- Example 3) Inline measuring of pressure during bulk filling

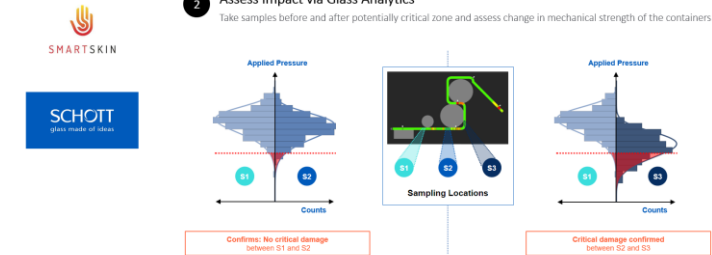
Impact of a Pre-flight Check



Verifying Need for Change

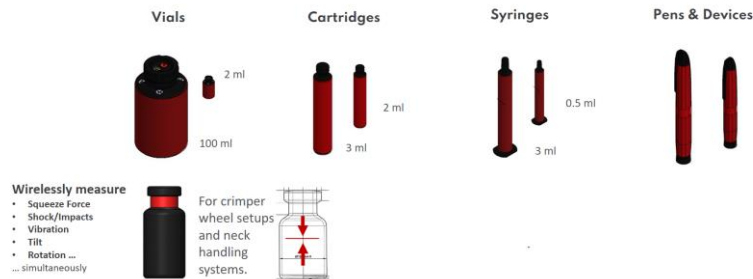
Software visualizes zones of higher forces, but no evidence on how the container reacts to it

- 1 Line Review via Sensor Drones
Screen line for elevated forces to identify potentially critical zones
- 2 Assess Impact via Glass Analytics
Take samples before and after potentially critical zone and assess change in mechanical strength of the containers



2022 Sensor Drone Portfolio

QUANTIFEEL Line of Force Sensors



This technology helps you controlling your line by visualizing what you can't see

Technology enables ...

- ✓ Systematic Line Optimization
- ✓ Maintenance and Setup Control

Technology proved benefit for ...

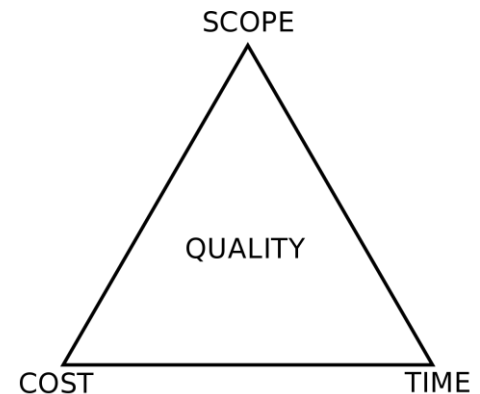
- ✓ Location of Origins for Glass Breakage
- ✓ Location of Origin for Cosmetic Damage
- ✓ Harmonization of Crimping (Heads/ Results)
- ✓ ... further application in preparation

Source: Smart Skin Technologies

Machine Use of Glass Primary Packaging Material

- **Summary**

- Technical concepts /solutions are available
- But there are limitations (“iron triangle”, “buying/selling standards”, company policies, space, ...)
- “New” can create other “disadvantages”
- Optimization vs. new concepts
- Recommendation: TR87 (2021)



Source: https://en.wikipedia.org/wiki/Project_management_triangle



PDA Technical Report No. 87 (TR 87)
Current Best Practices for Pharmaceutical
Glass Vial Handling and Processing

Questions?

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Syntegon Packaging Technology
Pharma liquid

