Machine Use of Glass Primary Packaging Material

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Pharma liquid

Machine Use of Glass Primary Packaging Material

Machine Runability

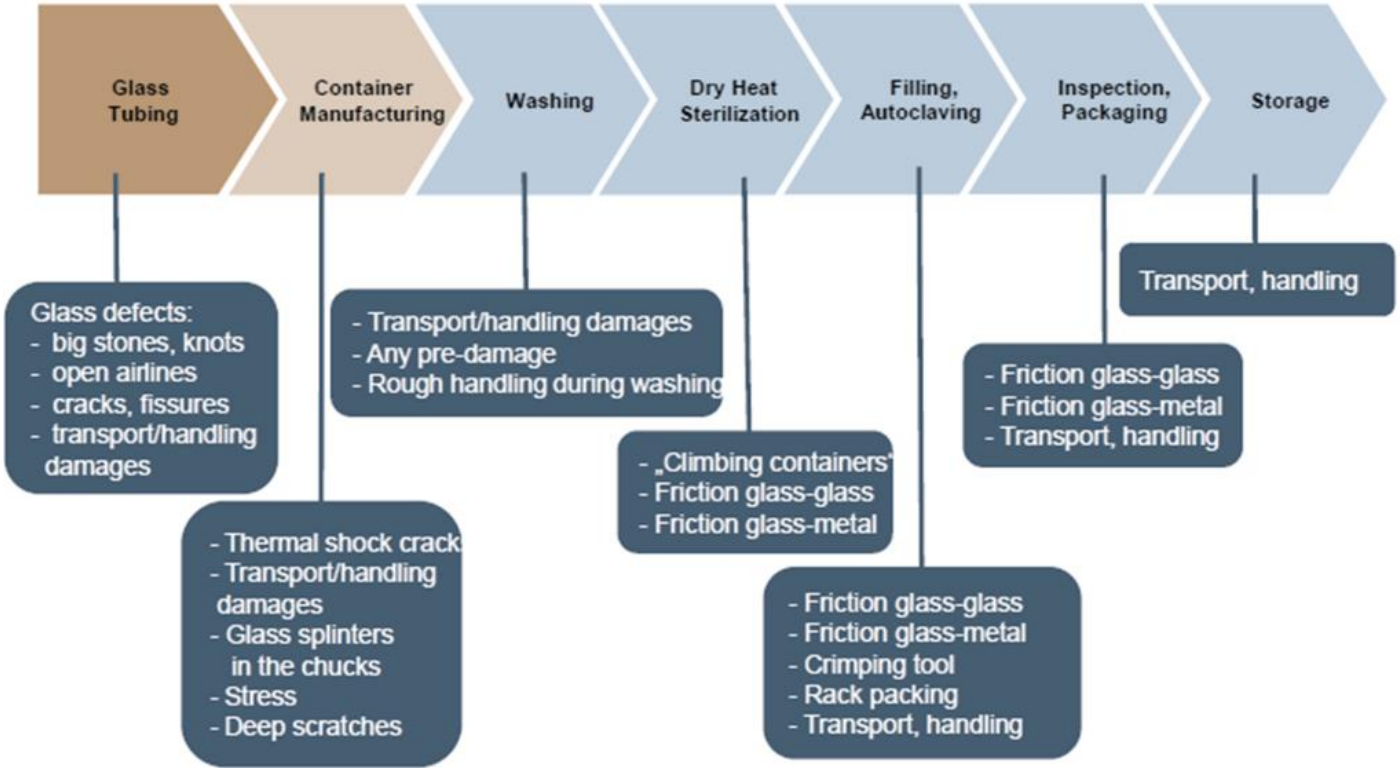
Machine Runability

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

Machine Runability

Breakage: Process Analysis

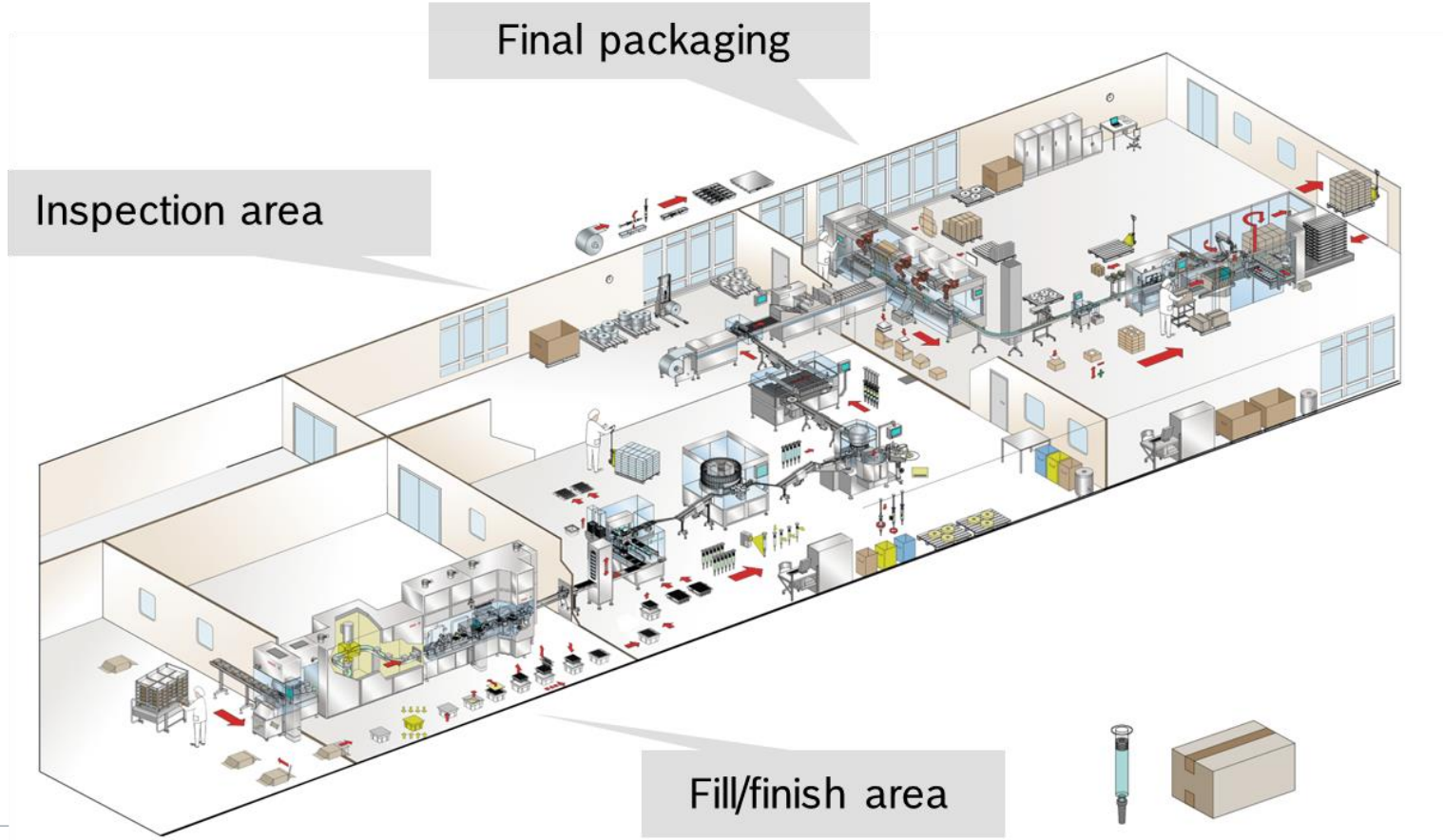
What can lead to breakage in the converting or filling process?



Source: Schott AG

Machine Runability

- **The way of a syringe/cartridge**



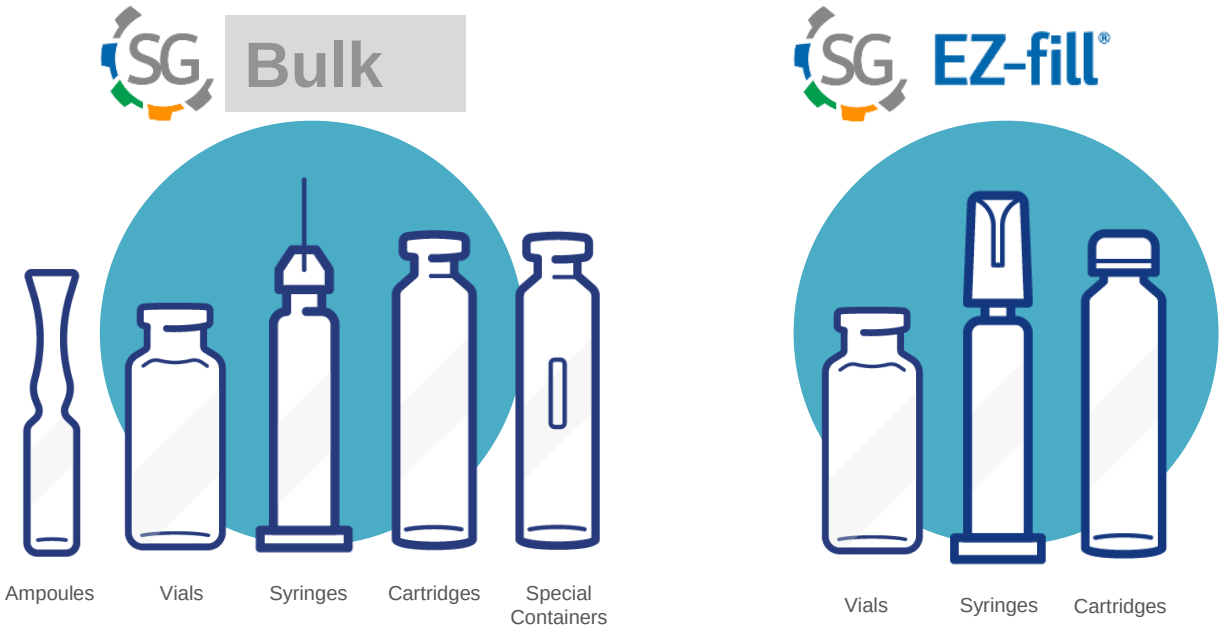
Machine Runability

- 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

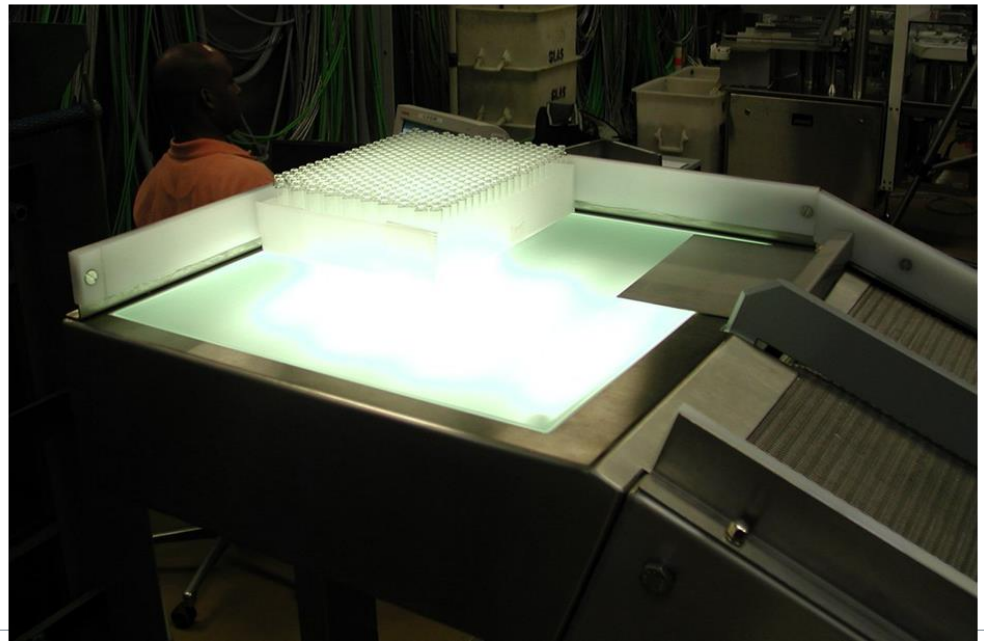
Machine Runability

- 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”

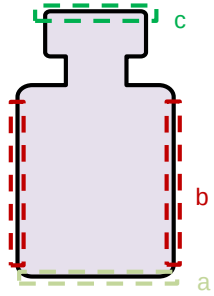


Machine Runability

- Empty vial inspection | Overview

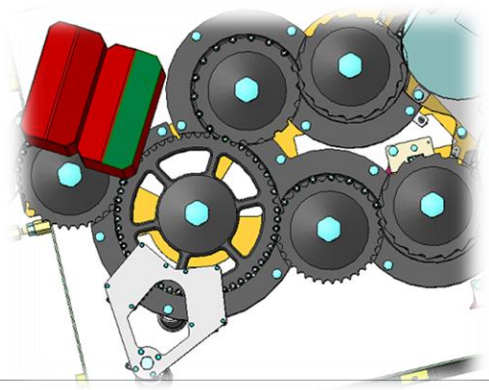
Inspection areas

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



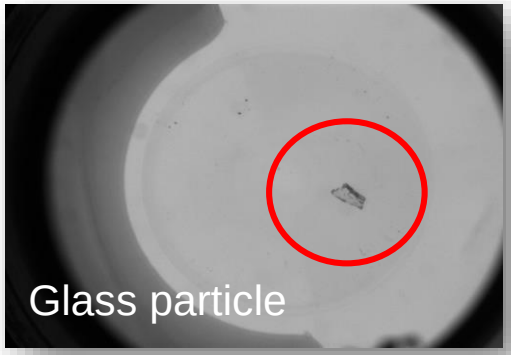
- Inspection of bottom + opening through vial opening (keyhole principal) with special optics each
- Inspection of sidewall with four cameras from the side
- Inspection for particles (e.g. splinters) and glass defects (e.g. scratches, cracks)
- Defect size ≥100µm

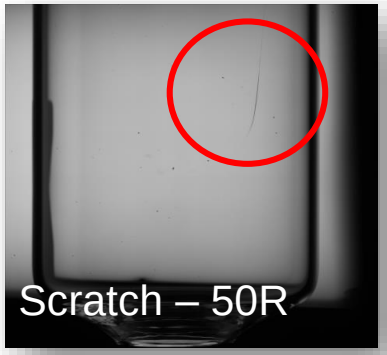
Bottom Opening Sidewall

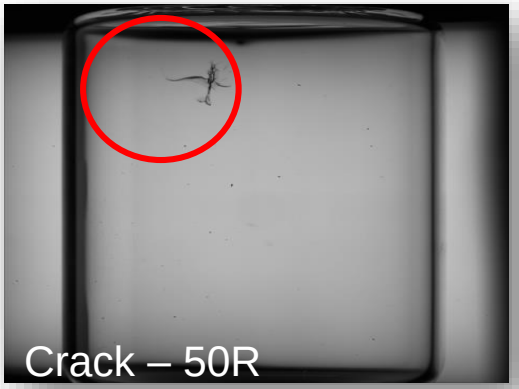


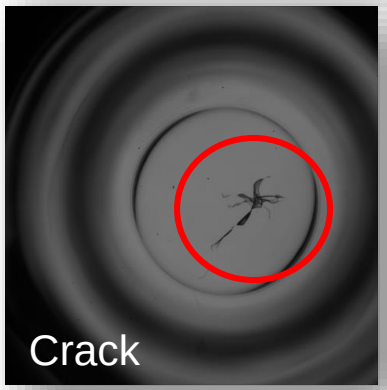
Machine Runability

- Empty vial inspection | Example images







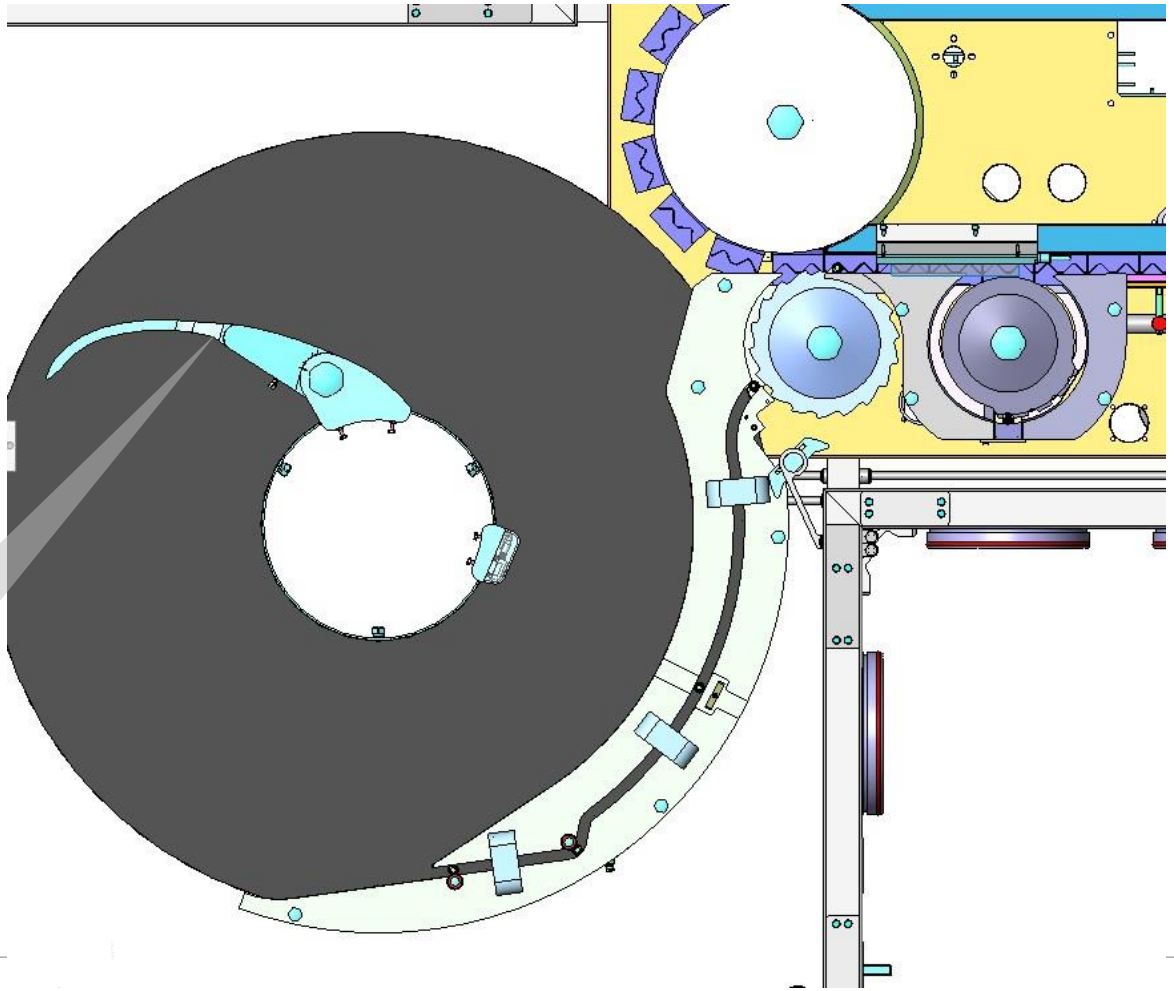


Machine Runability

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

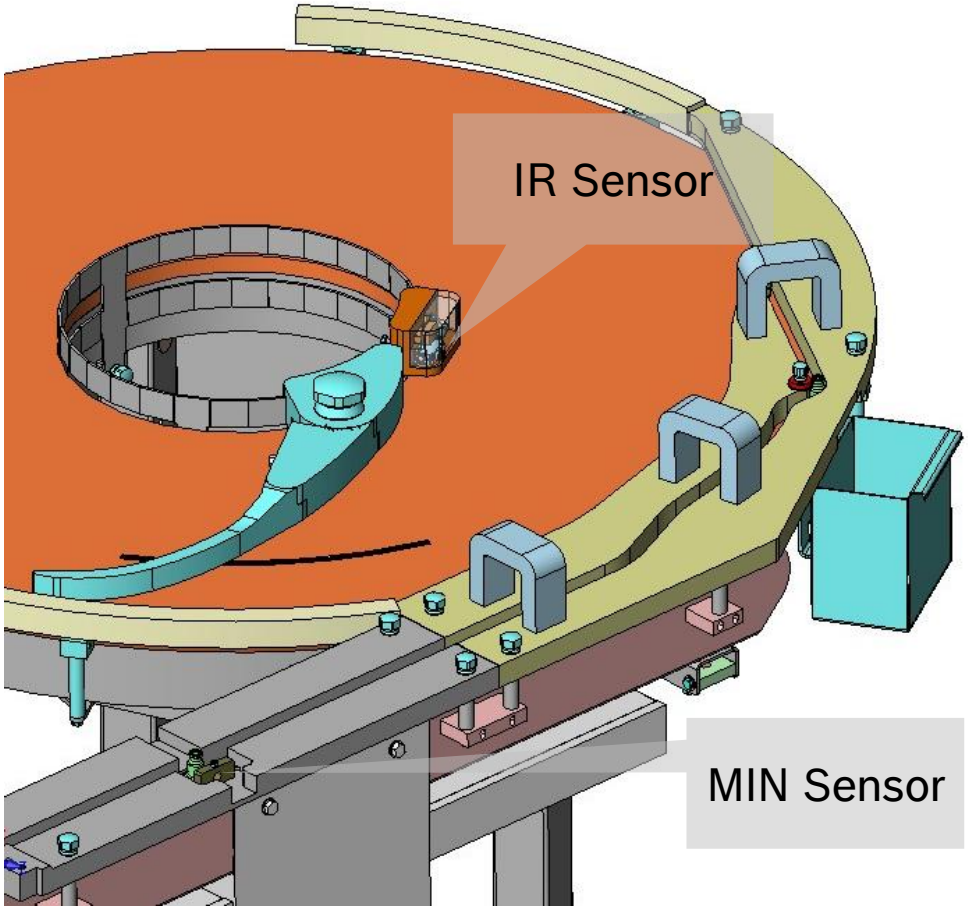
Practical Example: singularization of vials

Machine Runability



Flexible arm

Machine Runability



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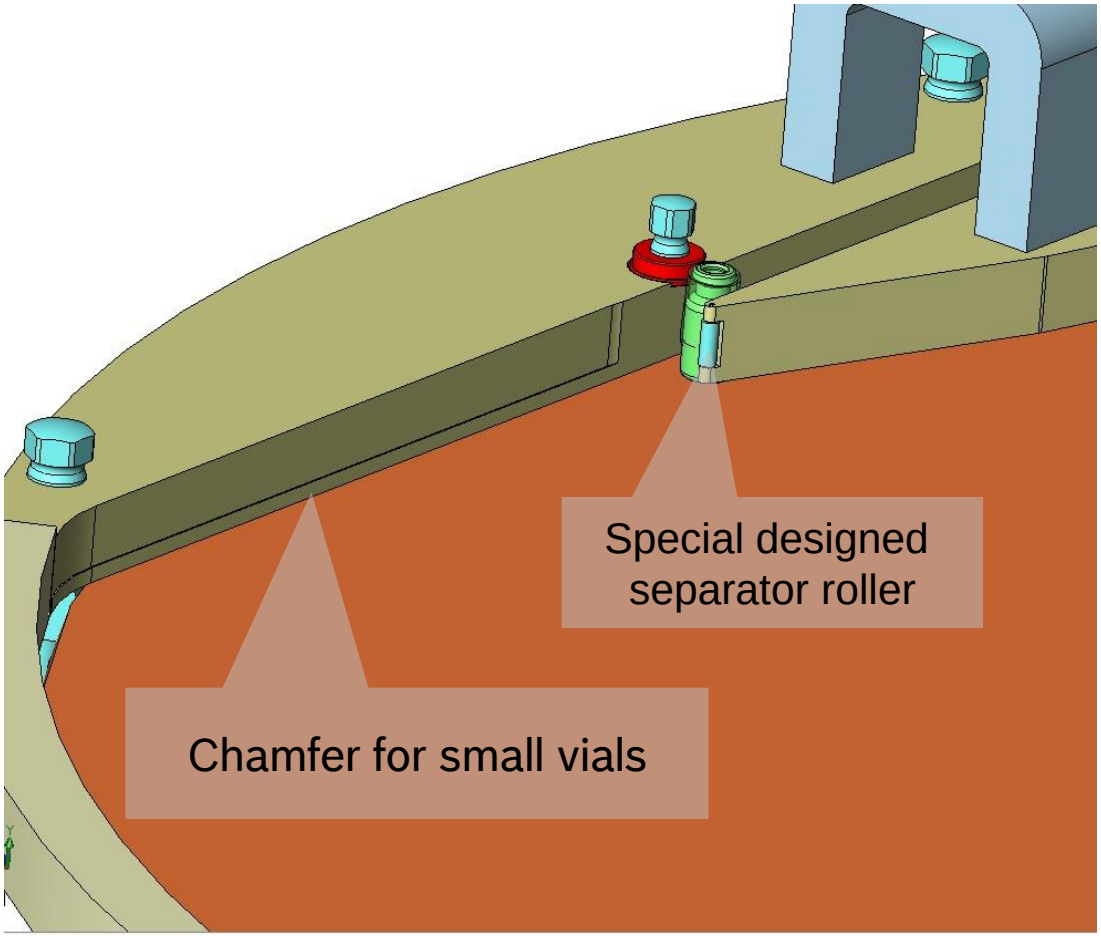

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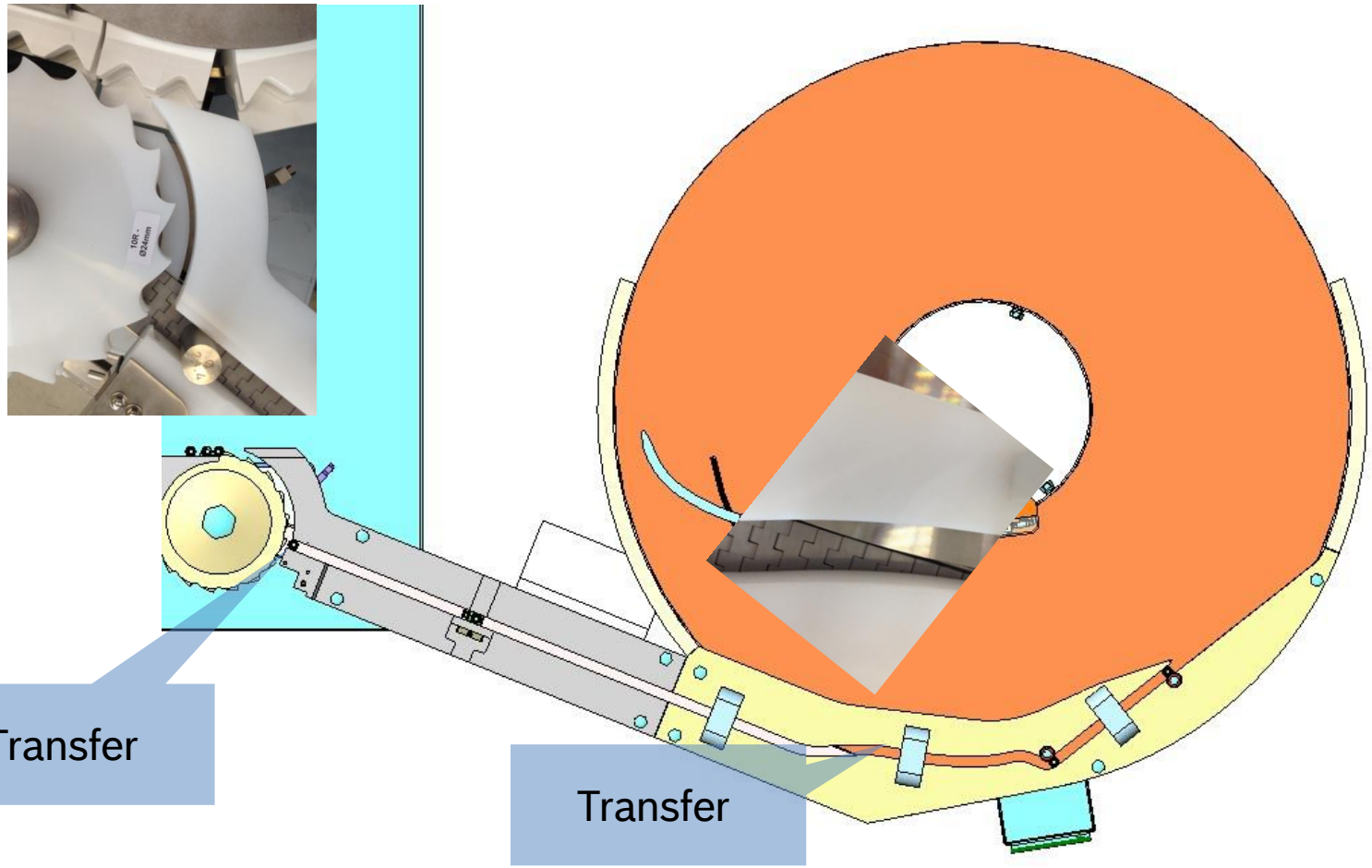

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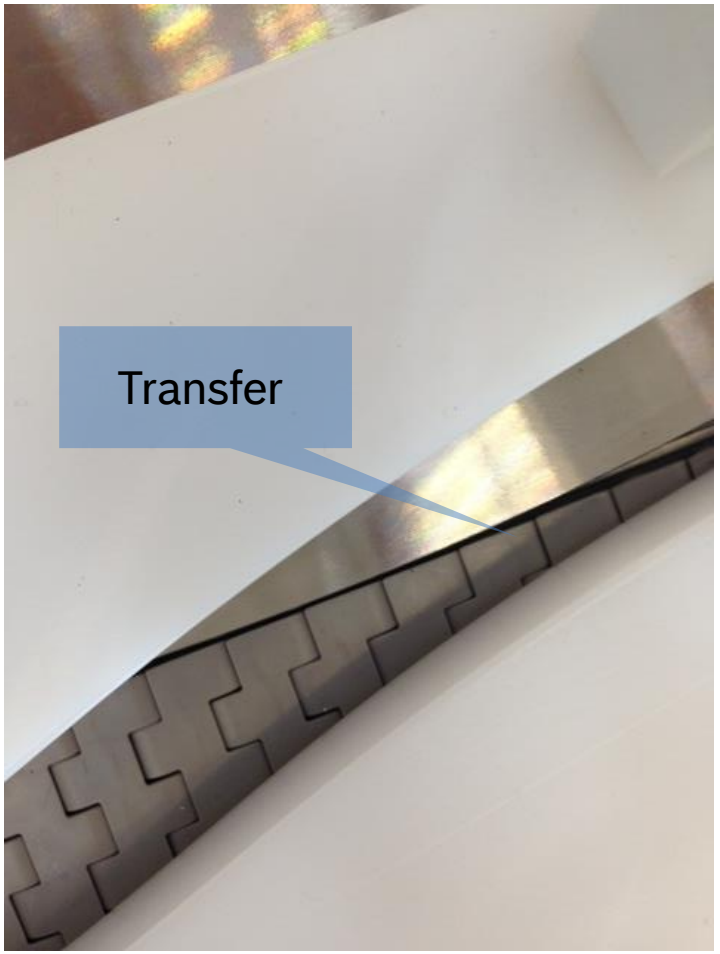


Machine Runability

- Tolerance of containers:
  - Design of size parts with play

- Roughness of containers :
  - Material composition and geometric adaption size parts:
    - Target: reduce friction

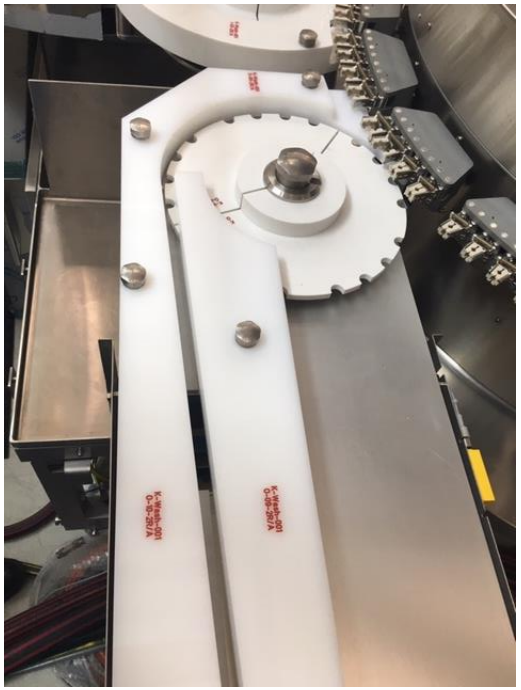
Machine Runability

- 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

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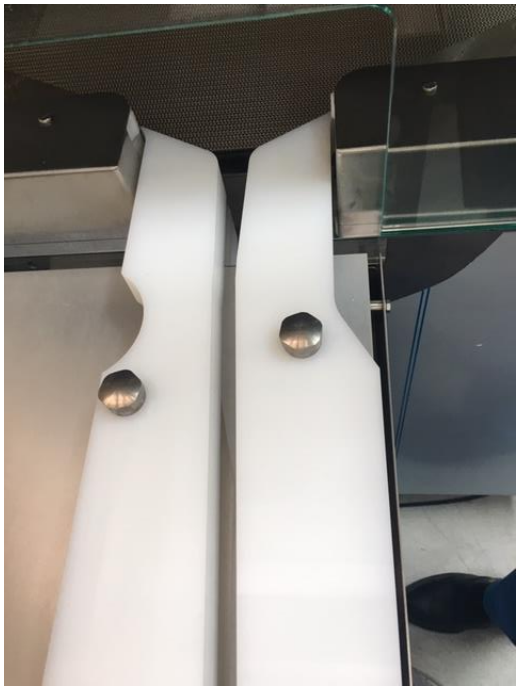
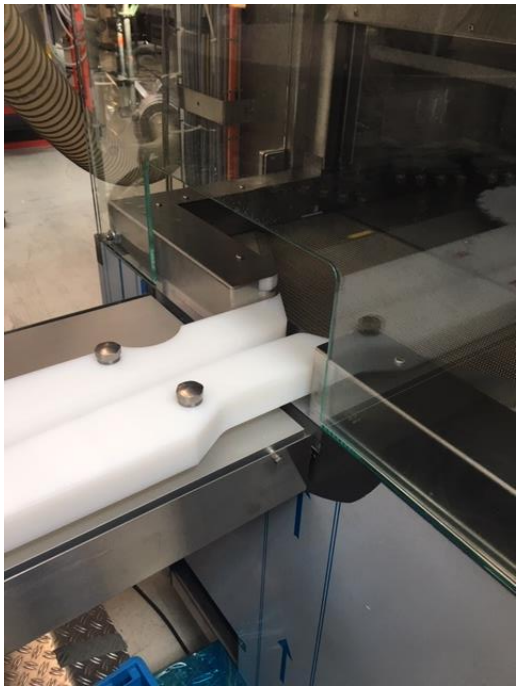




Machine Runability

- Tolerance of containers:
  - Design of size parts with play

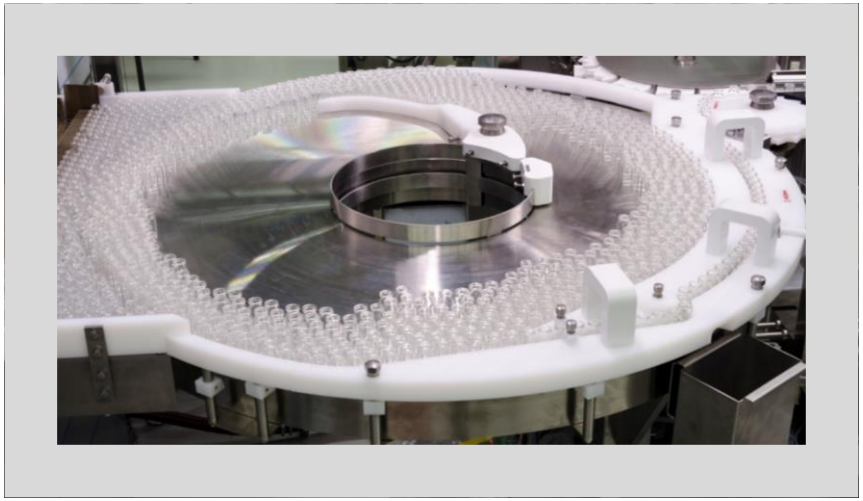
- Roughness of containers :
  - Material composition and geometric adaption size parts:
    - Target: reduce friction
  - Outer Coating of containers :
    - Silicone
    - Special containers: Corning
    - Special coated containers: Schott, SG, Gerresheimer, Corning, …*)

- Geometry of containers:
  - Single lane infeed vs. double lane infeed

* Only examples – listing not exhaustive

Machine Runability

- Single lane infeed vs. double lane infeed



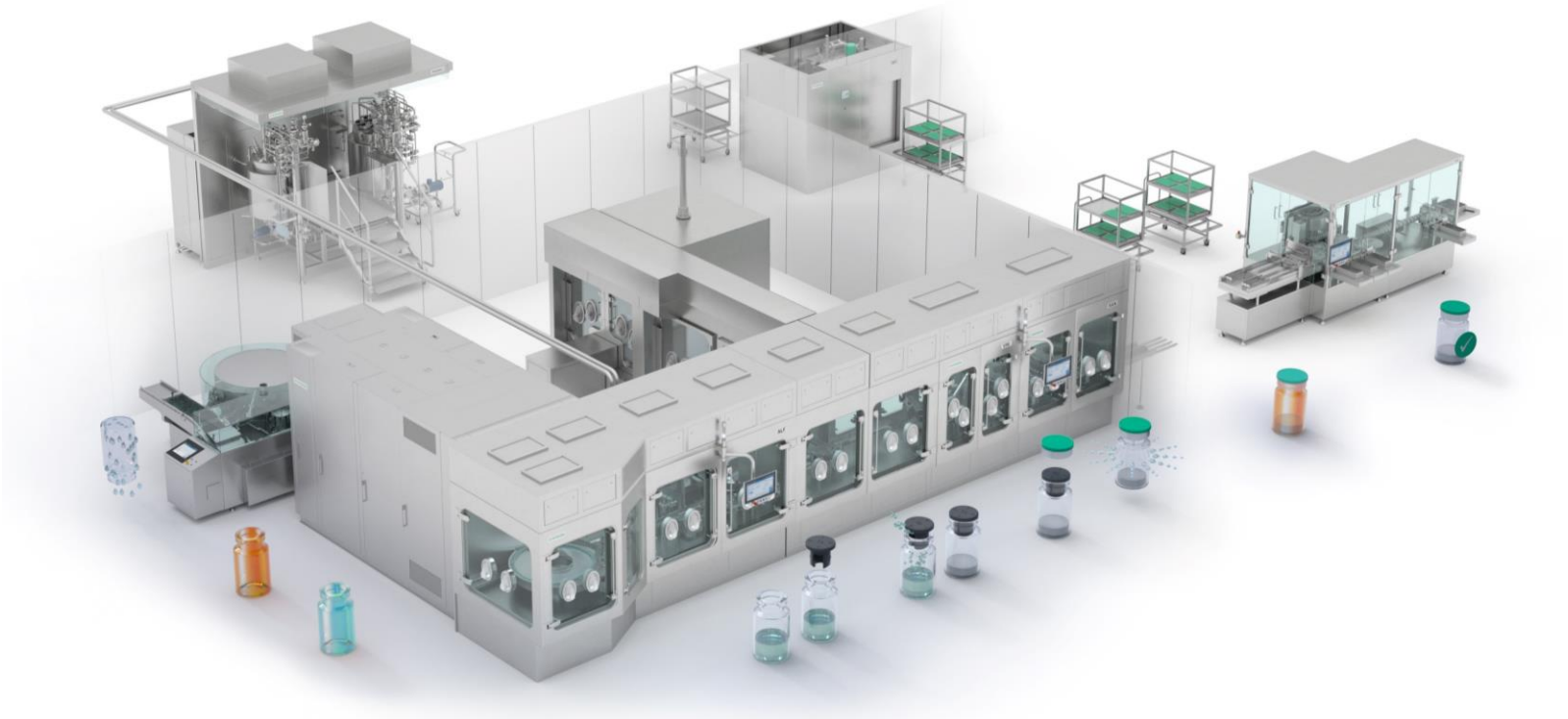
Machine Use of Glass Primary Packaging Material

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

Syntegon Packaging Technology | Business Unit Pharma | Markus Heinz (Product Manager)

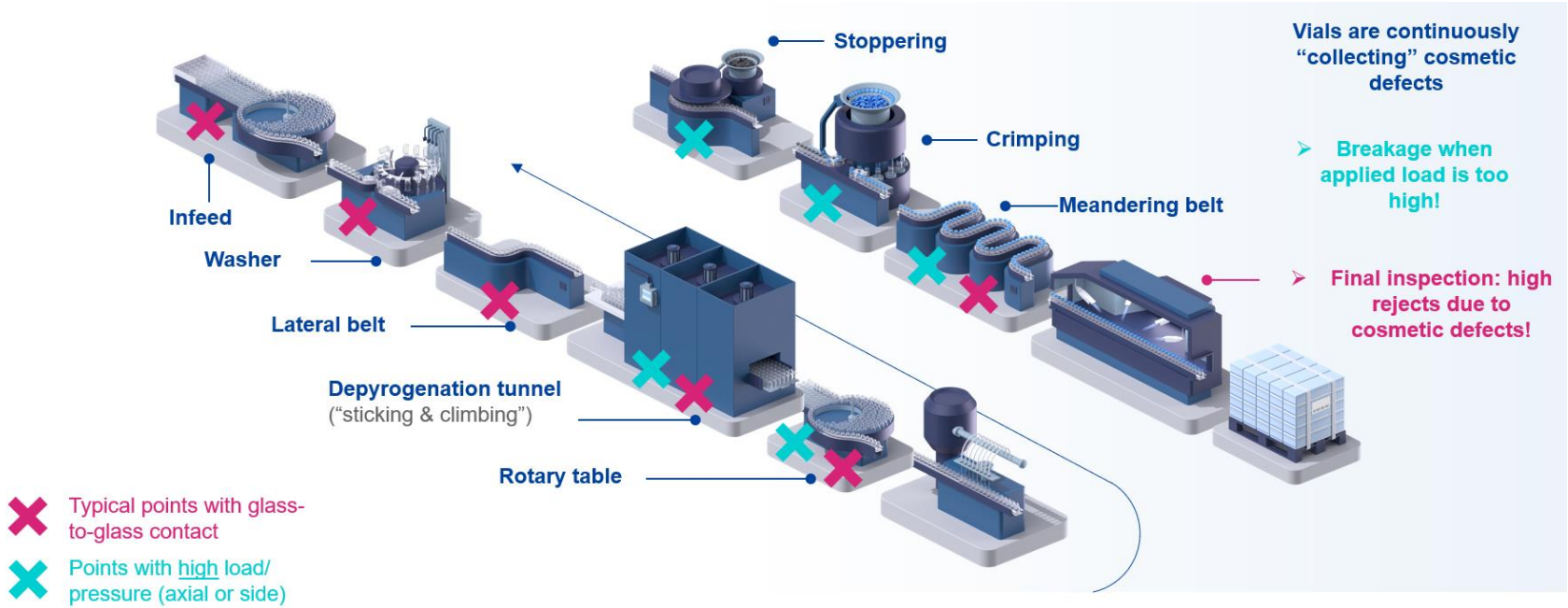
Along the Process Chain

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



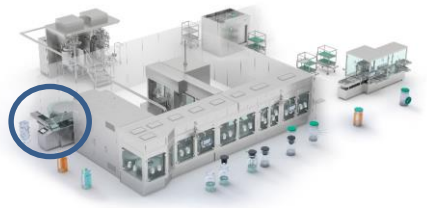
Along the Process Chain

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

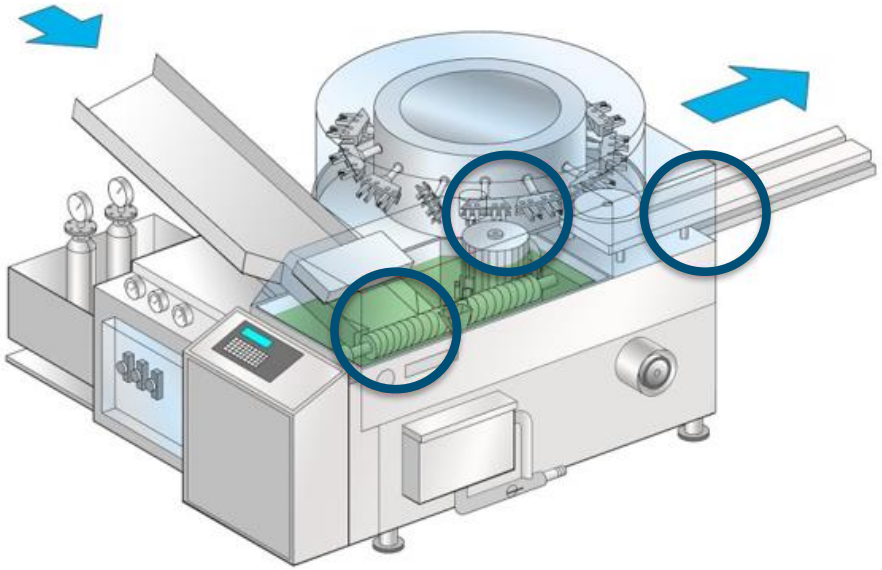


Source: SCHOTT AG

Along the Process Chain

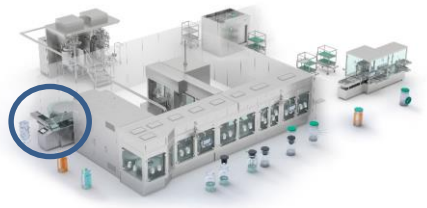


- **First step: Cleaning**

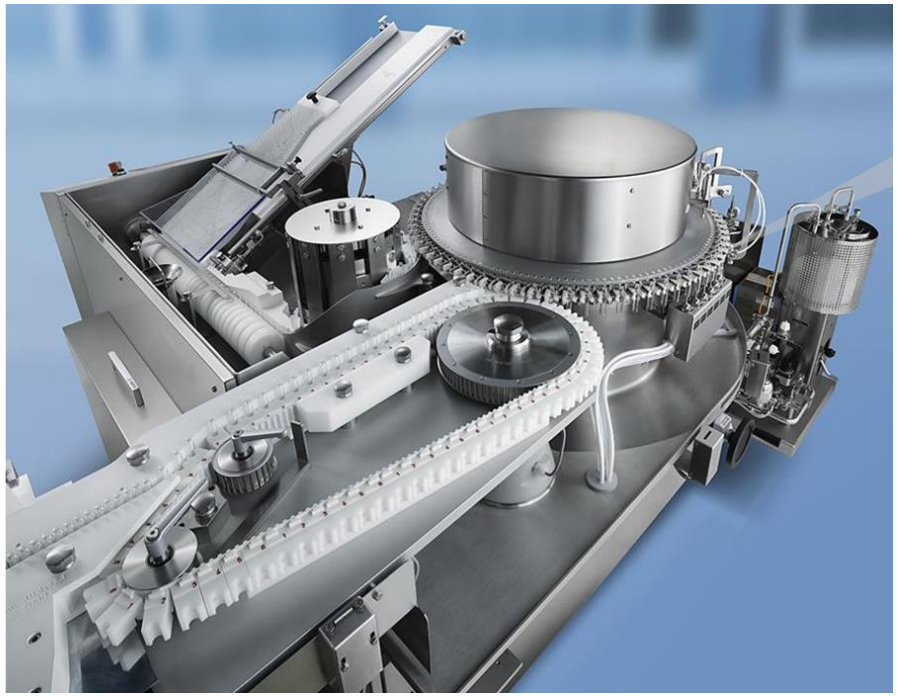


- **Critical areas – washing**
  - Bulk infeed and singularization
  - Needle for water and sterile air entering into containers several times
  - Glass-to-glass contact at handover to sterilizing tunnel

Along the Process Chain

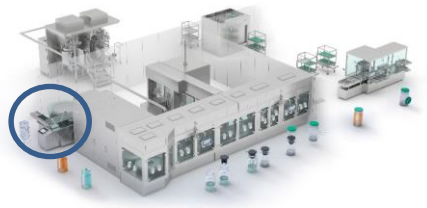


- **First optional step: Siliconizing**



- **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

Single lane feeding to tunnel

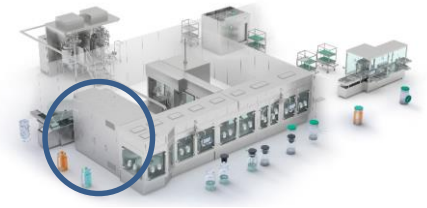
Scroll conveyer system incl. jam protection

Ultrasonic bath

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

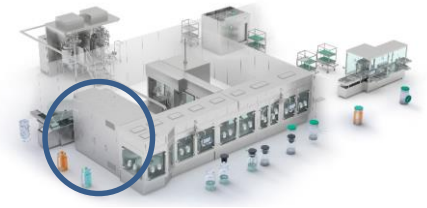
Along the Process Chain

- **Important transfer: Sterilization & Depyrogenation**



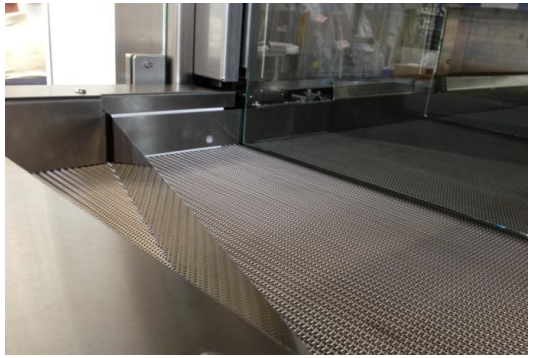
- **Critical areas –** Sterilization
  - Direct glass-to-glass contact within the system
  - Pressure on containers in tunnel infeed section
  - Heating of glass containers up to >300 degrees Celsius
  - Reduction/destruction of the water skin of the glass → sticky and scratch sensitive containers

Along the Process Chain



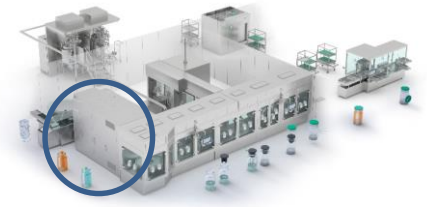
- **Important transfer: Sterilization & Depyrogenation**

  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**

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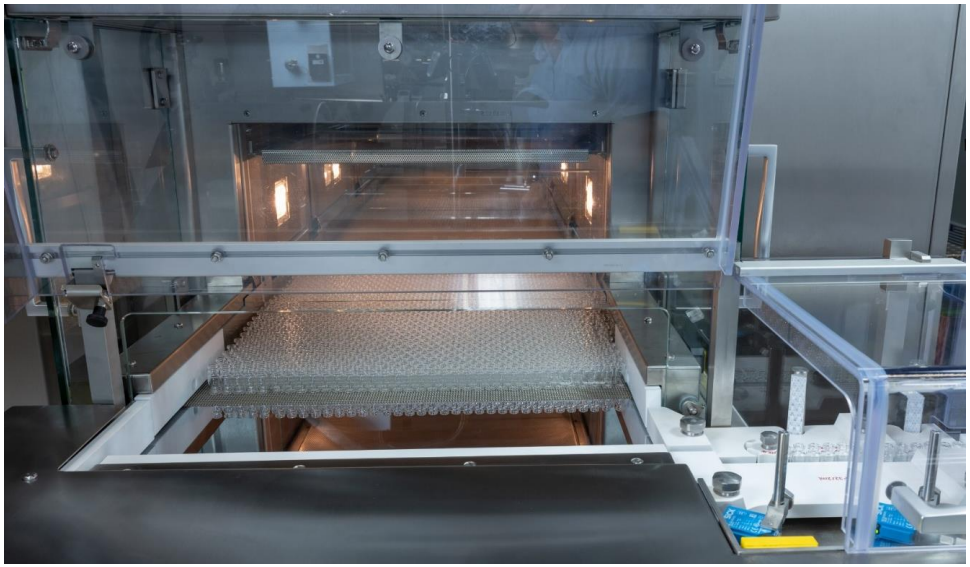
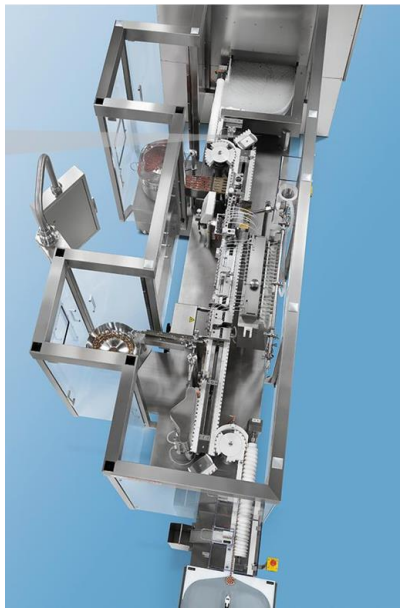
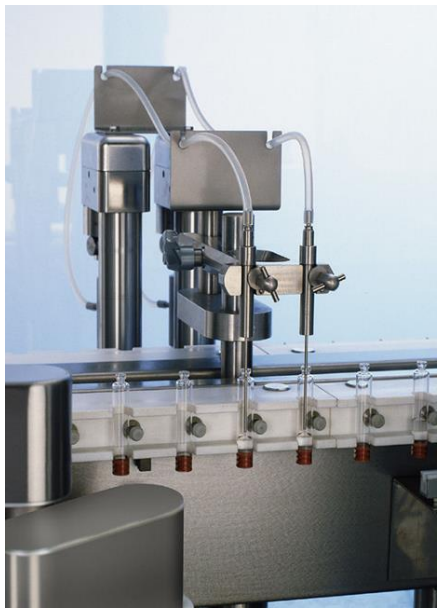


Row by Row – Loading Zone

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-ø 3,15 ± 0,2 mm
      - Filling needle outer-ø 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**

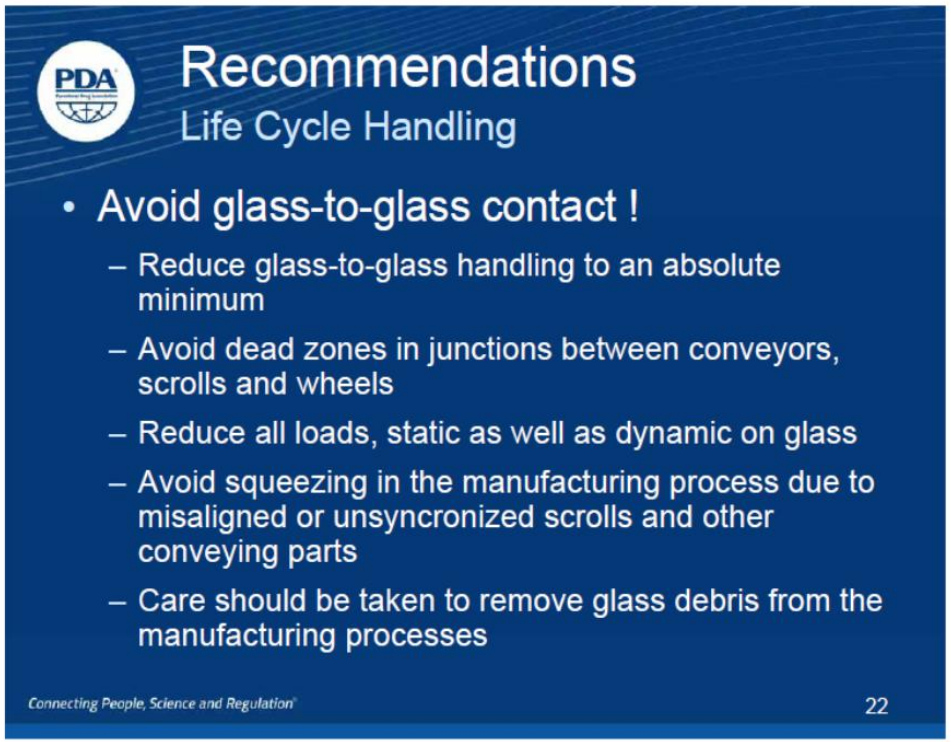
Solutions for less stress on the glass

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?



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

Syntegon Packaging Technology | Business Unit Pharma | Markus Heinz (Product Manager)

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

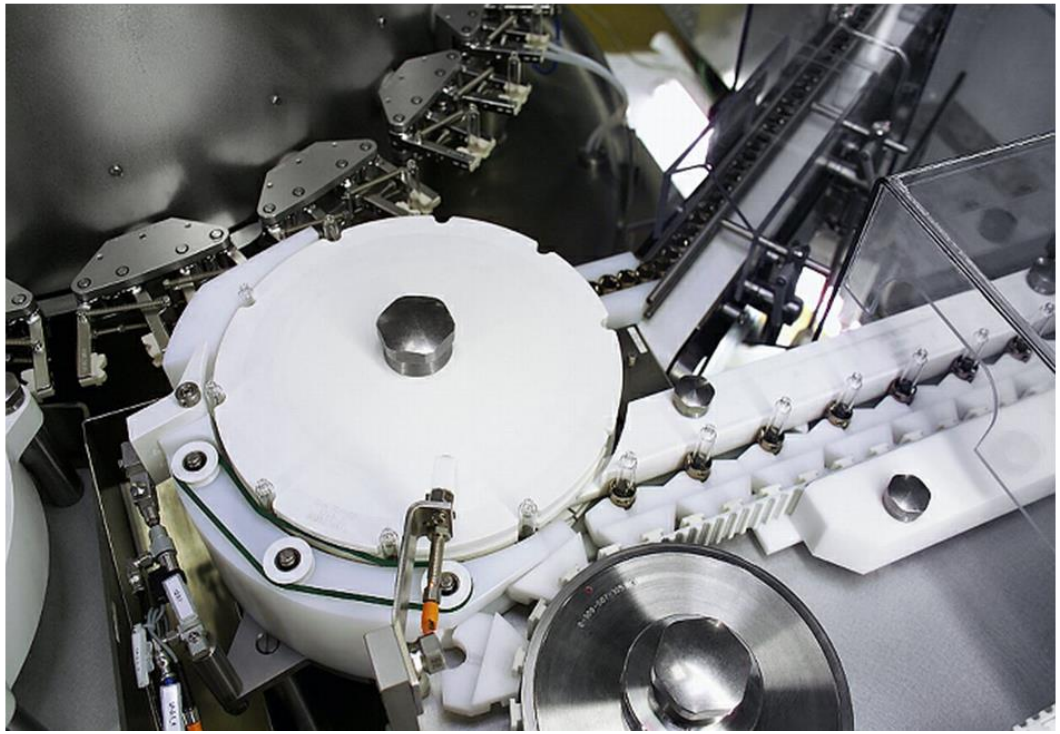
- Robotic feeding

Problems and solutions

- Stainless steel transport pucks

Problems and solutions

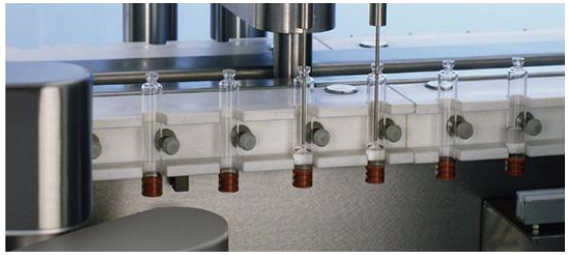
- Washer outfeed/tunnel infeed - detail



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

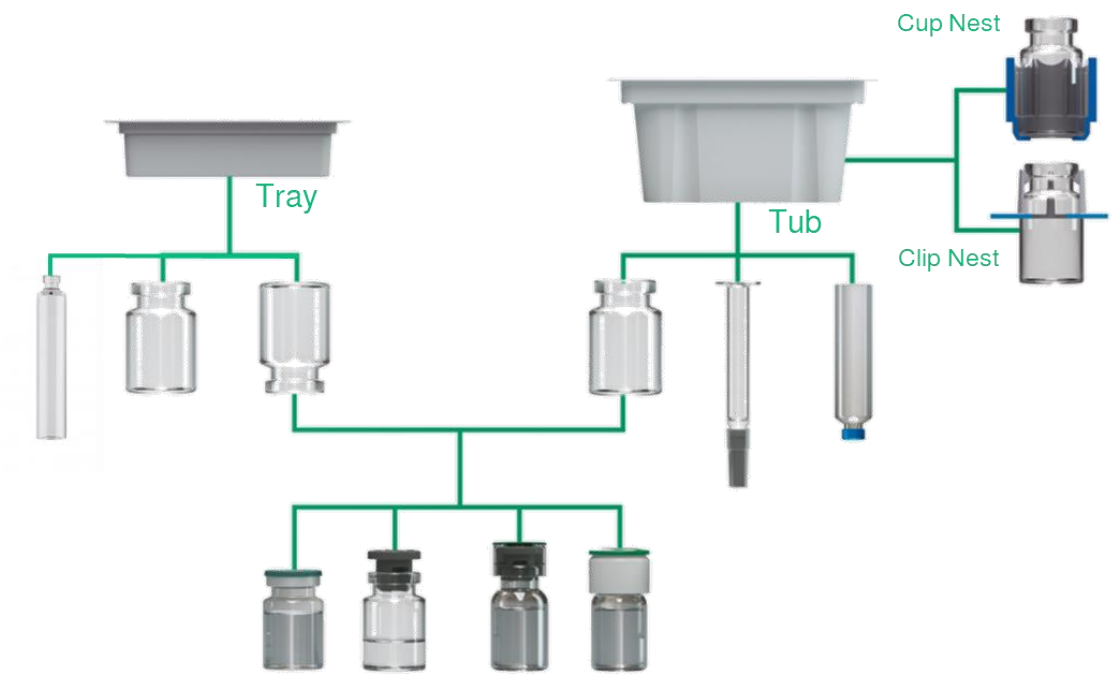
- Infeed with robotic systems and transport tray

Problems and solutions

- Infeed filling machine with transport pucks

Problems and solutions

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



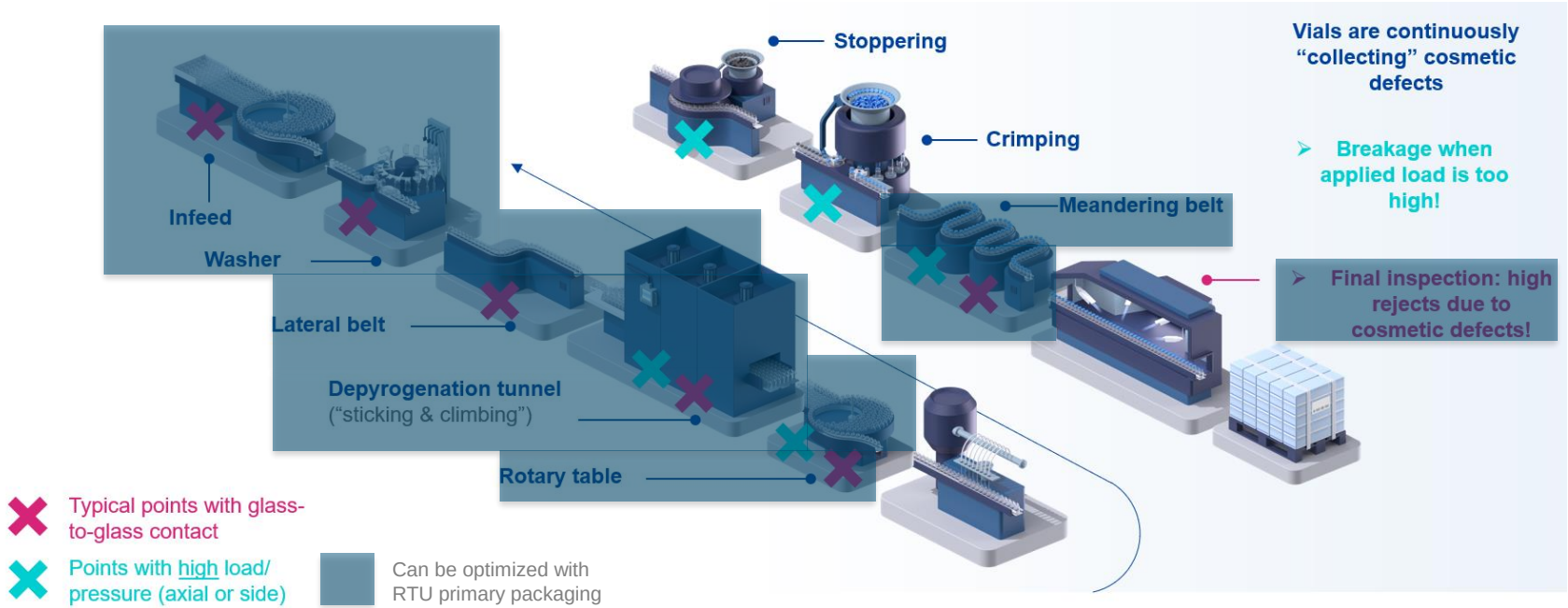
NO glass-to-glass contact - secondary packaging should preserve:

- 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

filling & closing

Nested syringes

Centering plate stainless steel

Problems and solutions

- Example: tub/nest processing for syringes

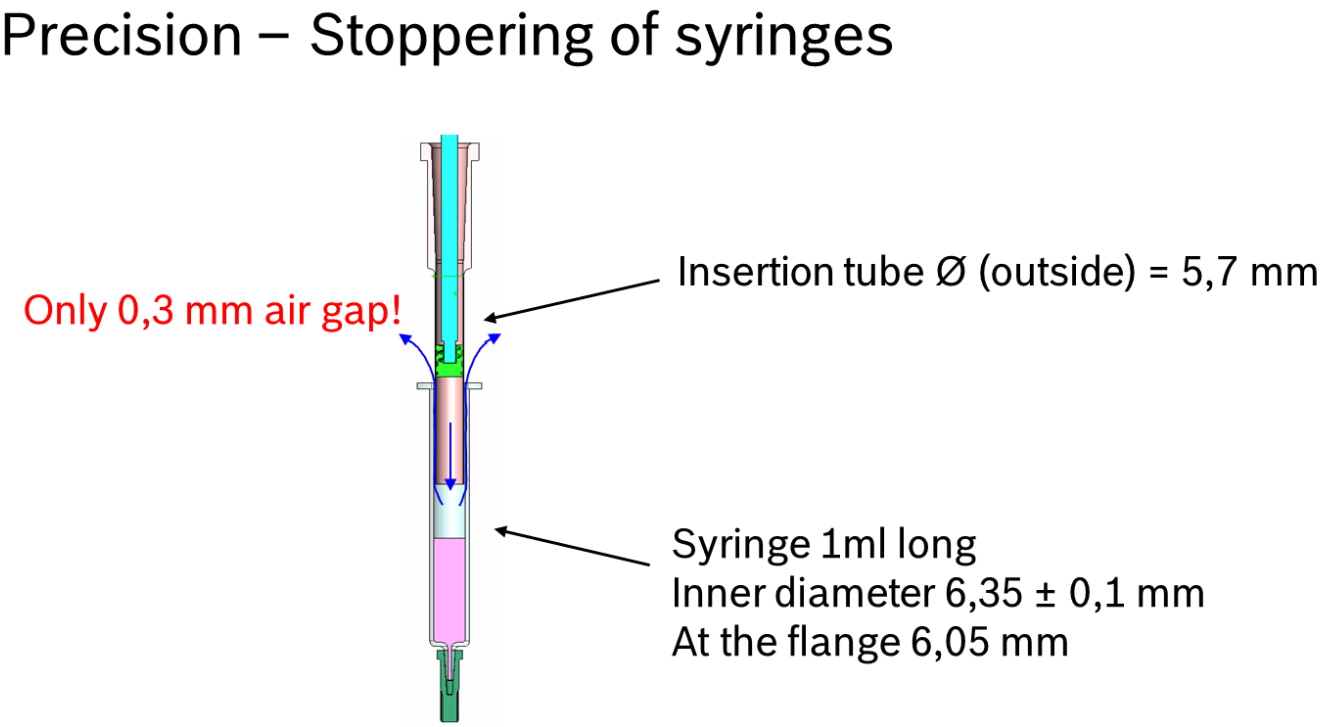
filling & closing

Nested syringes – alternative centering plate

Centering plate plastic material

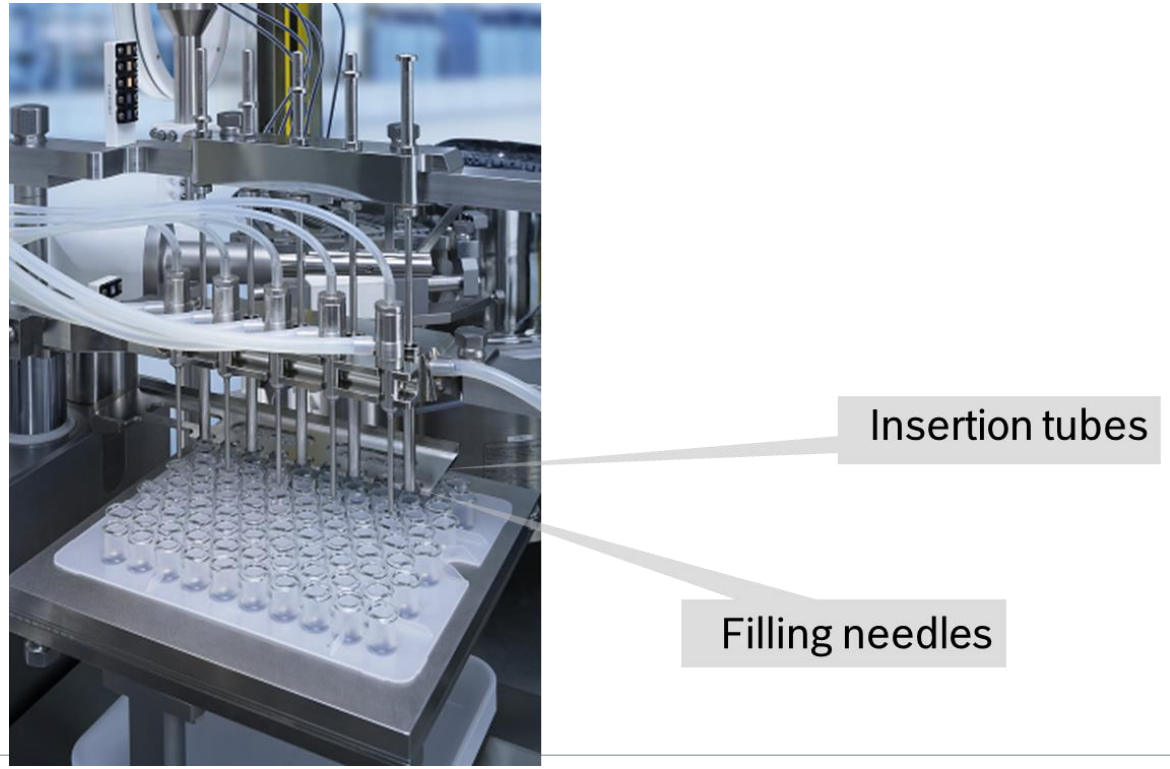
Problems and solutions

- Example: tub/nest processing for syringes



Problems and solutions

- Example: tub/nest processing for syringes



Problems and solutions

- Example: tub/nest processing for vials

Problems and solutions

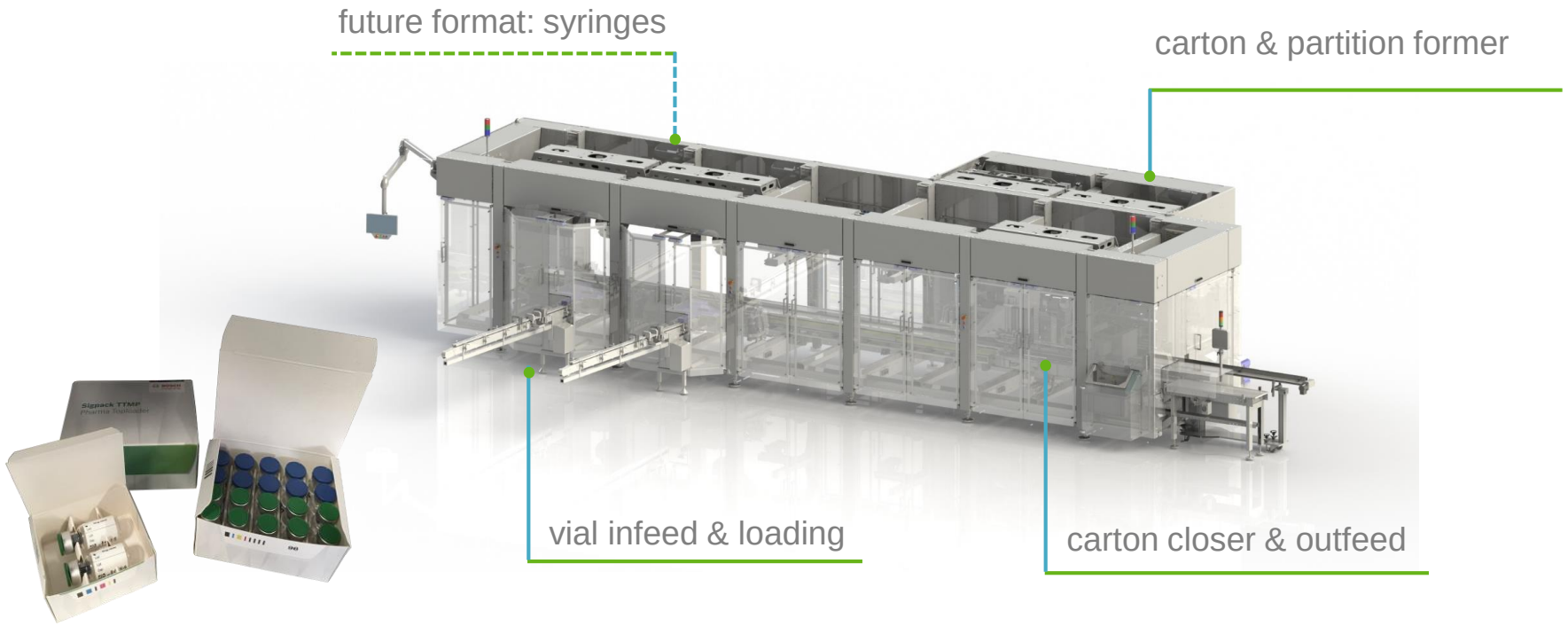
- Example downstream syringe: rod insertion and labeling

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

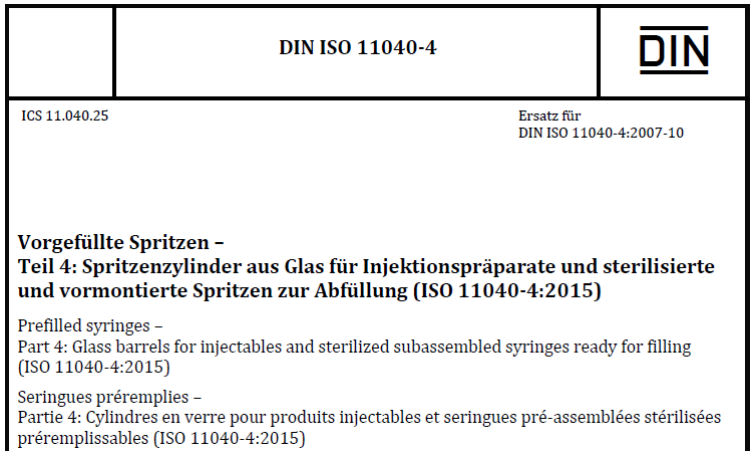
Coordination & Cooperation

- Cooperation is key

Source: Depositphotos

Coordination & Cooperation

- **Norms** – hard to unite BUT they help in collaboration



DIN ISO 11040-4

DIN

ICS 11.040.25

Ersatz für
DIN ISO 11040-4:2007-10

Vorgefüllte Spritzen –
Teil 4: Spritzenzylinder aus Glas für Injektionspräparate und sterilisierte und vormontierte Spritzen zur Abfüllung (ISO 11040-4:2015)

Prefilled syringes –
Part 4: Glass barrels for injectables and sterilized subassembled syringes ready for filling (ISO 11040-4:2015)

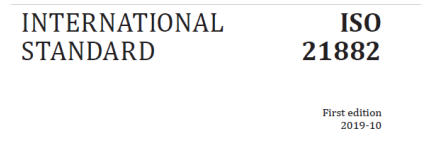
Seringues préremplies –
Partie 4: Cylindres en verre pour produits injectables et seringues pré-assemblées stérilisées prêtes à remplir (ISO 11040-4:2015)

INTERNATIONAL STANDARD **ISO 21881**

First edition
2019-10

Sterile packaged ready for filling glass cartridges

Cartouches en verre préremplissables sous emballage stérile

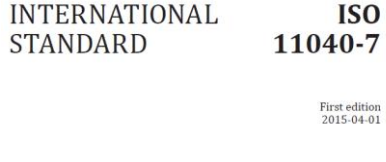


INTERNATIONAL STANDARD **ISO 21882**

First edition
2019-10

Sterile packaged ready for filling glass vials

Flacons en verre préremplissables sous emballage stérile

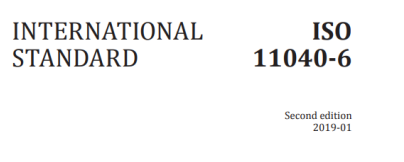


INTERNATIONAL STANDARD **ISO 11040-7**

First edition
2015-04-01

Prefilled syringes —

Part 7:
Packaging systems for sterilized subassembled syringes ready for filling



INTERNATIONAL STANDARD **ISO 11040-6**

Second edition
2019-01

Prefilled syringes —

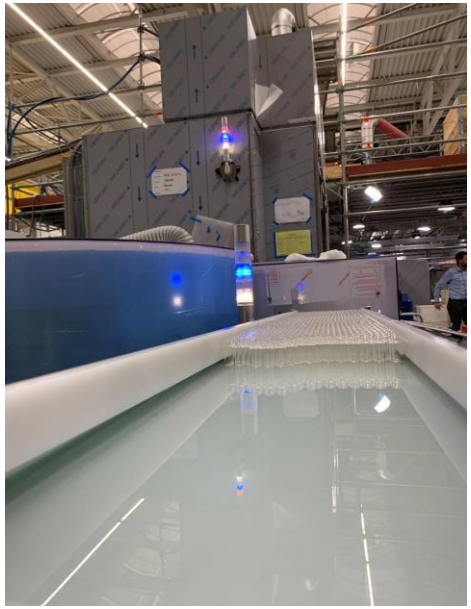
Part 6:
Plastic barrels for injectables and sterilized subassembled syringes ready for filling

Coordination & Cooperation

- **Example 1) Cooperation in design of new packaging materials**

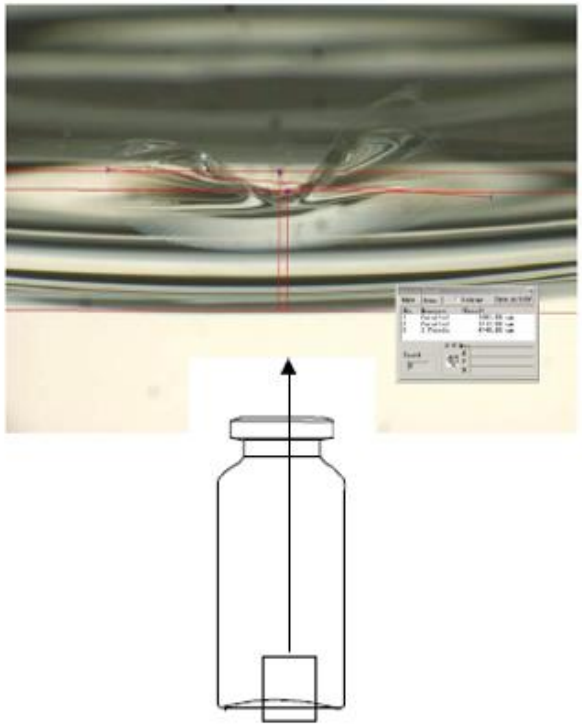
  Example: Common machine test:
  - Vial line (speed washer-tunnel-filler 500 vials per minute, speed capper 600 vials per minute) for 2R vials ø 16 +/- 0,15 mm
  - Tested vials:
    - **Valor vials:** ø 16,75 mm +/- 0,25 mm
    - **Coated Borosilicate vials:** ø 16,5 mm +/- 0,2 mm
    - **Borosilicate vials:** ø 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

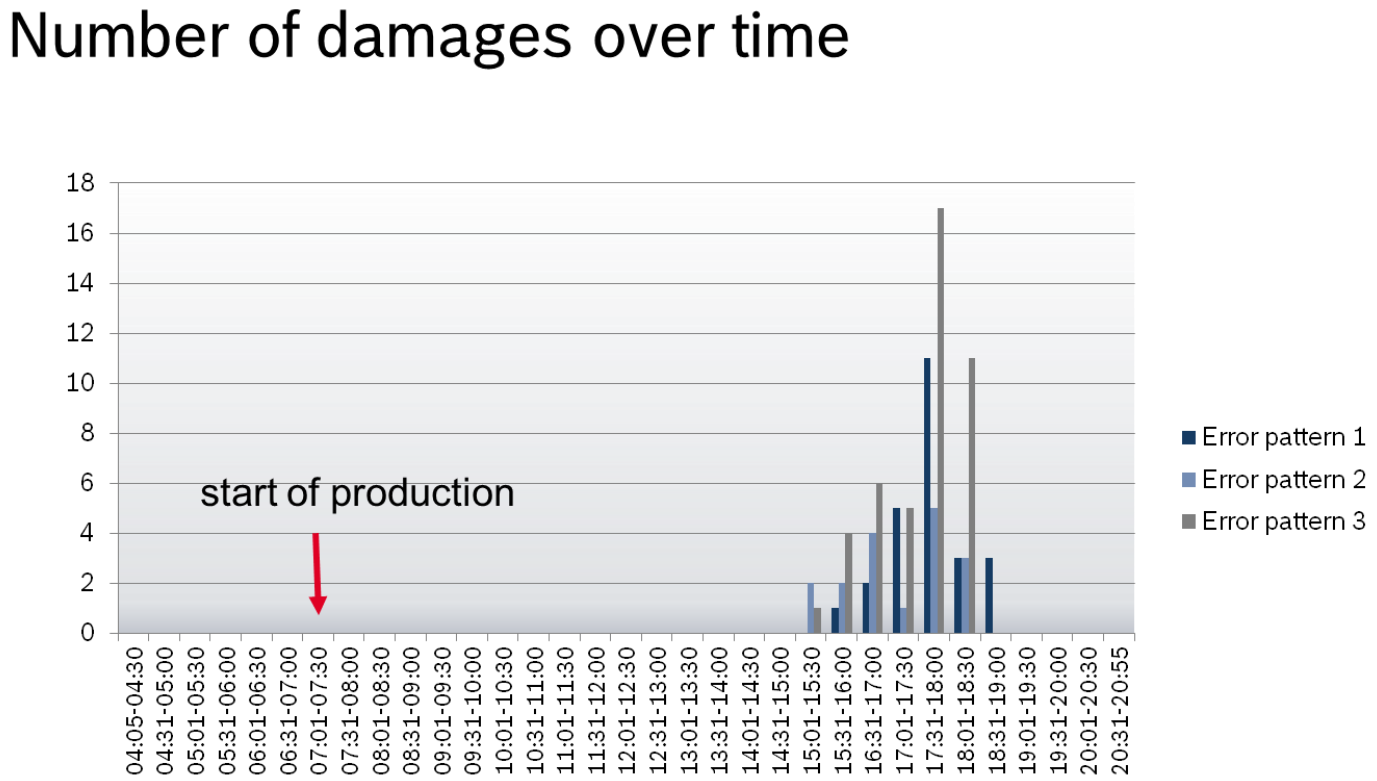
- **Example 2) Common route cause analysis in case of failures**
  - Case study at customer: vials damaged in bottom area



- **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

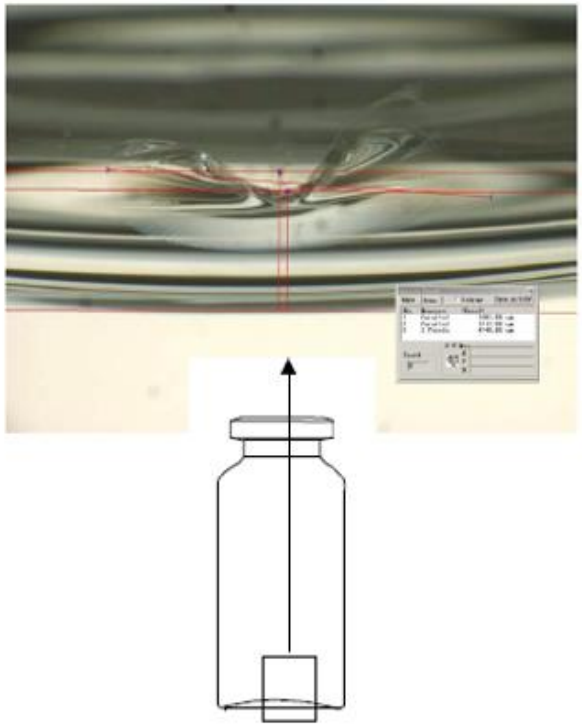
Coordination & Cooperation

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



Coordination & Cooperation

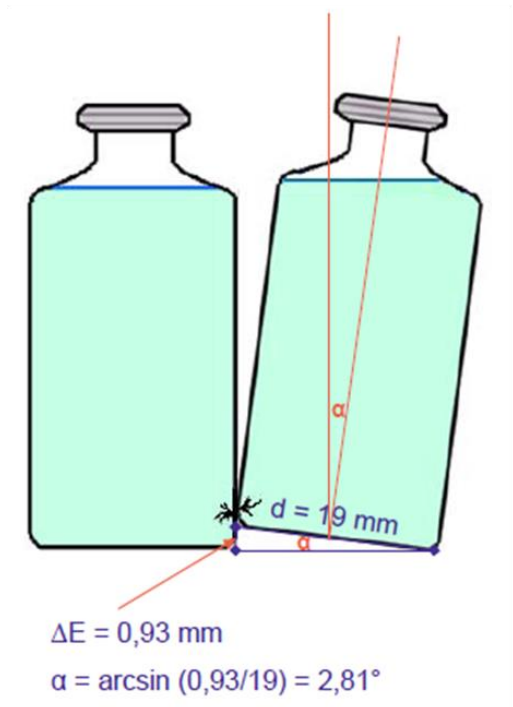
- **Example 2) Common route cause analysis in case of failures**
  - Case study at customer: vials damaged in bottom area



- **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**

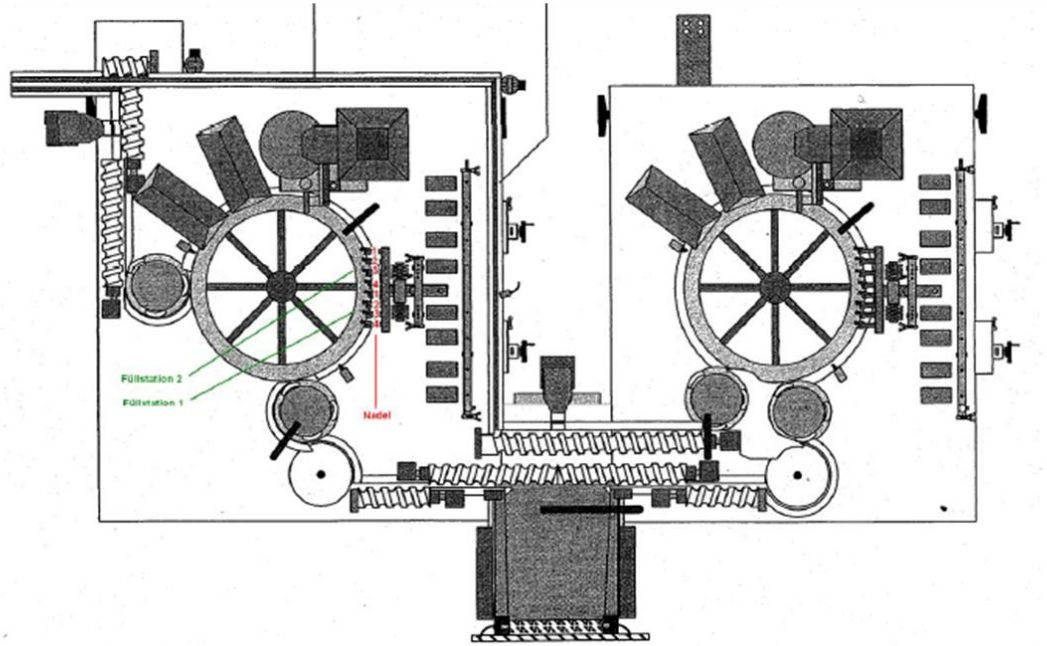
Crash constellation

Coordination & Cooperation

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

Machine layout

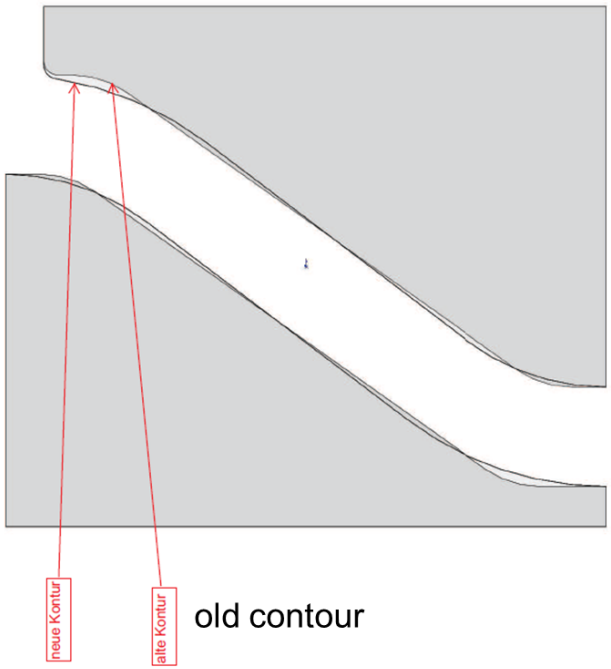
Critical spot:
Scroll onto a belt



Coordination & Cooperation

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

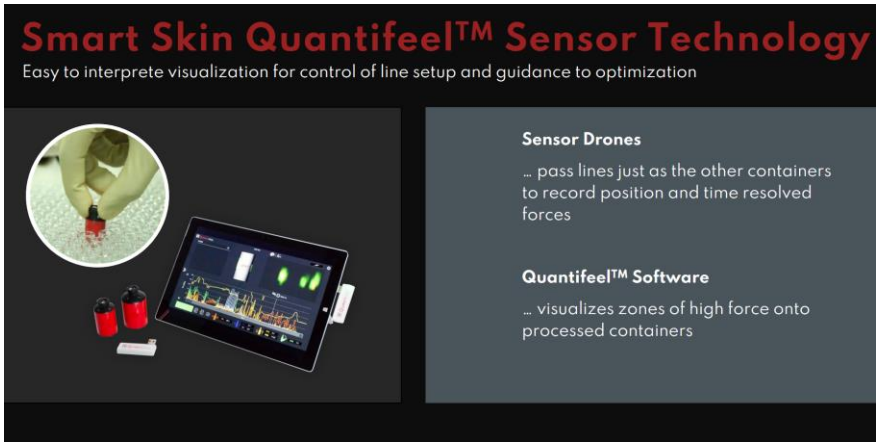
New sizepart at outfeed

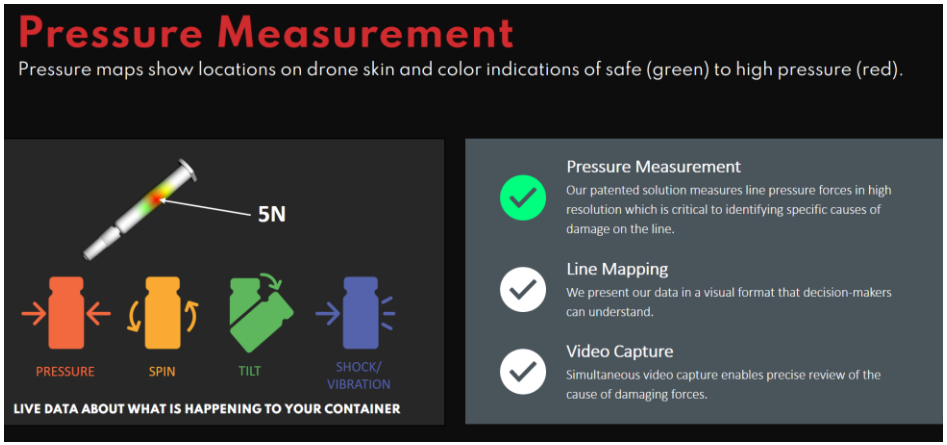


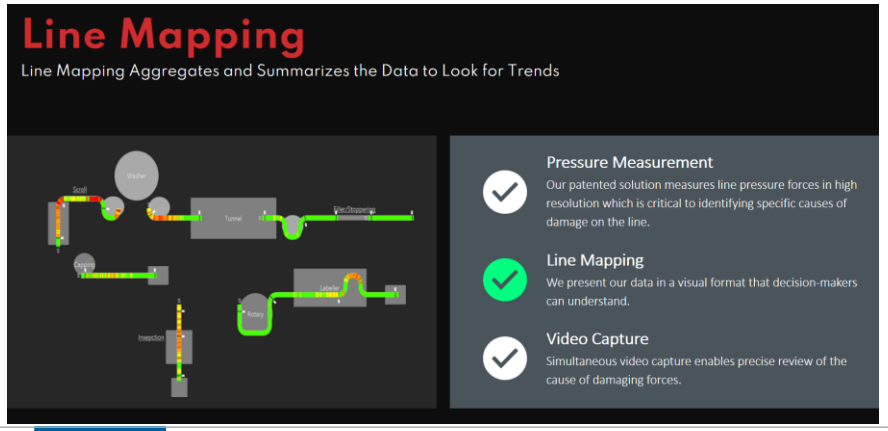
Small change ➔ huge effect

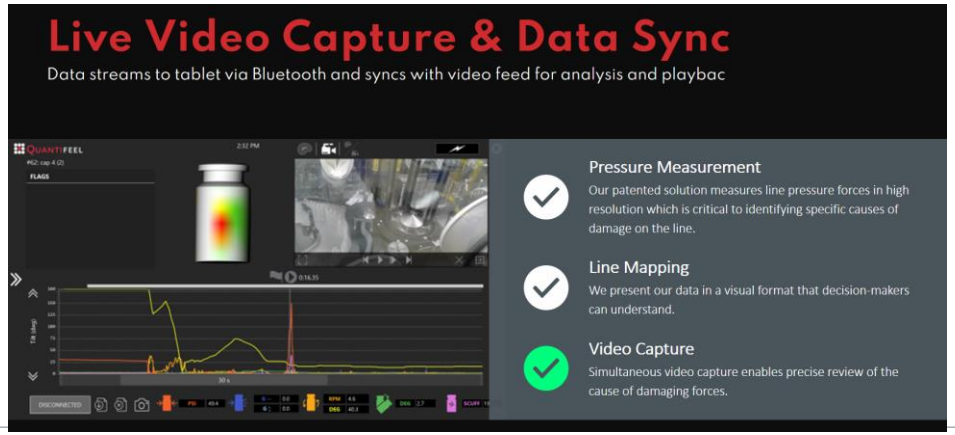
Coordination & Cooperation

- **Example 3) Inline measuring of pressure during bulk filling**





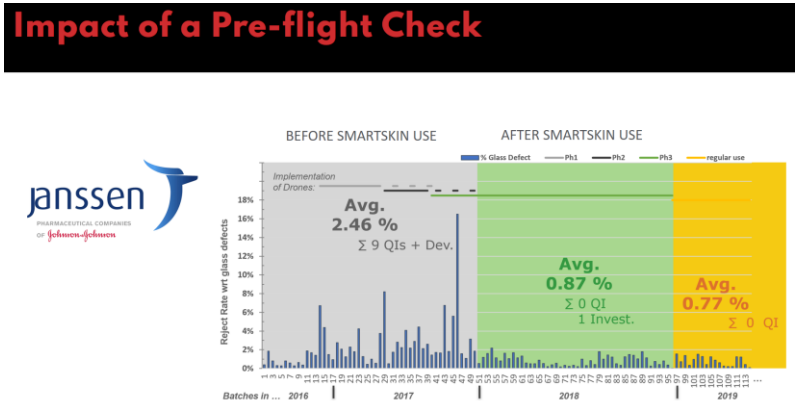


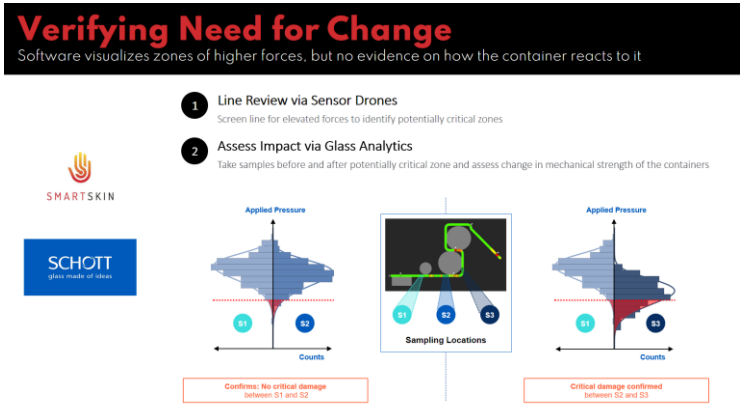


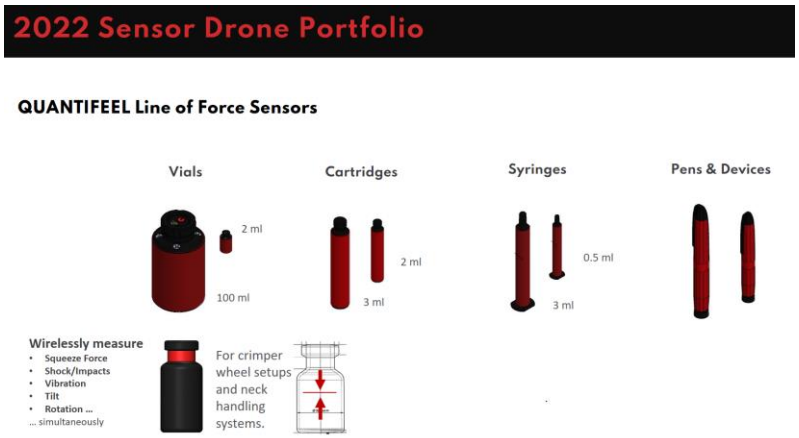
Source: Smart Skin Technologies

Coordination & Cooperation

- Example 3) Inline measuring of pressure during bulk filling





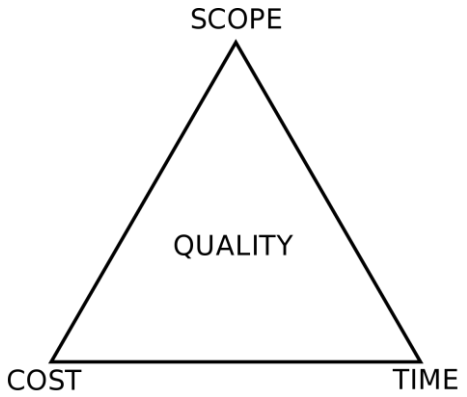


Source: Smart Skin Technologies

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)

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



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

Questions?

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Global Product Manager
Syntegon Packaging Technology
Pharma liquid