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Parenteral Drug Association

Mainz, 18./19.10.2017

Training course glass

Klaus Ullherr, Senior Product Manager, Bosch Packaging Technology, Pharma liquid

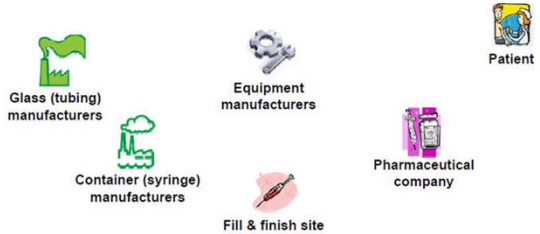


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Machine impact on containers

The Stakeholders



- Glass (tubing) manufacturers
- Equipment manufacturers
- Patient
- Container (syringe) manufacturers
- Fill & finish site
- Pharmaceutical company

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

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Breakage: Process Analysis

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

The diagram illustrates the following stages and associated breakage causes:

- Glass Tubing:**
 - Glass defects:
 - big stones, knots
 - open airlines
 - cracks, fissures
 - transport/handling damages
- Container Manufacturing:**
 - Thermal shock cracks
 - Transport/handling damages
 - Glass splinters in the chucks
 - Stress
 - Deep scratches
- Washing:**
 - Transport/handling damages
 - Any pre-damage
 - Rough handling during washing
- Dry Heat Sterilization:**
 - Climbing containers
 - Friction glass-glass
 - Friction glass-metal
- Filling, Autoclaving:**
 - Friction glass-glass
 - Friction glass-metal
 - Crimping tool
 - Rack packing
 - Transport, handling
- Inspection, Packaging:**
 - Friction glass-glass
 - Friction glass-metal
 - Transport, handling
- Storage:**
 - Transport, handling

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The way of a syringe/cartridge

The diagram shows the layout of a manufacturing facility with the following key areas:

- Fill/finish area:** Located at the bottom of the facility, where the syringes or cartridges are initially prepared.
- Inspection area:** A central area where the products are checked for quality and safety.
- Final packaging:** The end of the production line where the finished products are packaged for distribution.


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Where is impact on the glass?



Cartridge processing

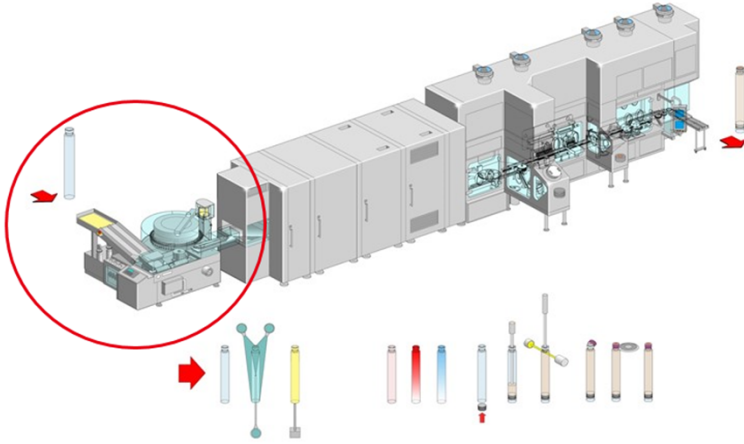
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Machine impact on containers

Critical areas – Washing & Siliconizing



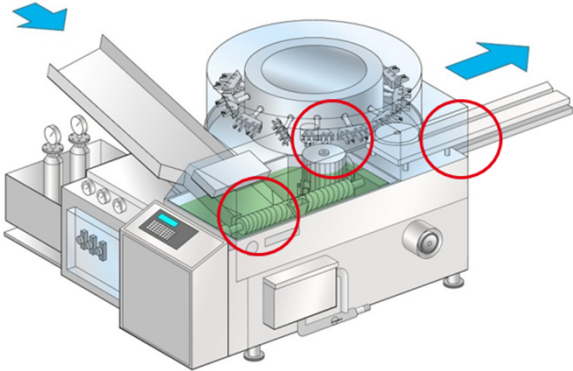
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Machine impact on containers

Critical areas – Washing & Siliconizing



- Bulk infeed and singularization
- Needles entering into Containers several times
- Glass to Glass Contact at handover to Sterilizing Tunnel

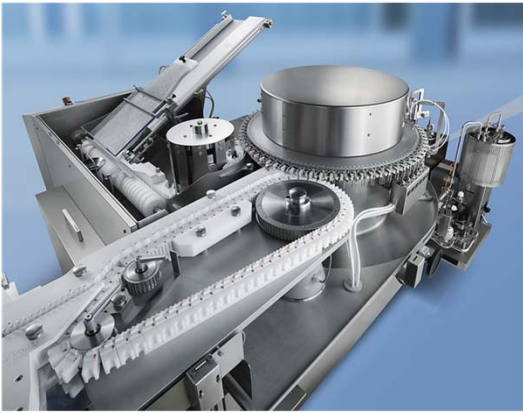
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Where is impact on the glass?



Needles for water and silicone are entering into the container

Cartridge processing, cleaning and transfer to sterilization

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Solutions – Washing & Siliconizing

- Servo ensures precise and reproducible needle movement
- Single feeding to Tunnel
- Scroll conveyor System incl. jam protection
- Ultrasonic bath
- Infeed magazine on a scroll conveyor → safer singularization especially in high output

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Special solution for detecting glass breakage

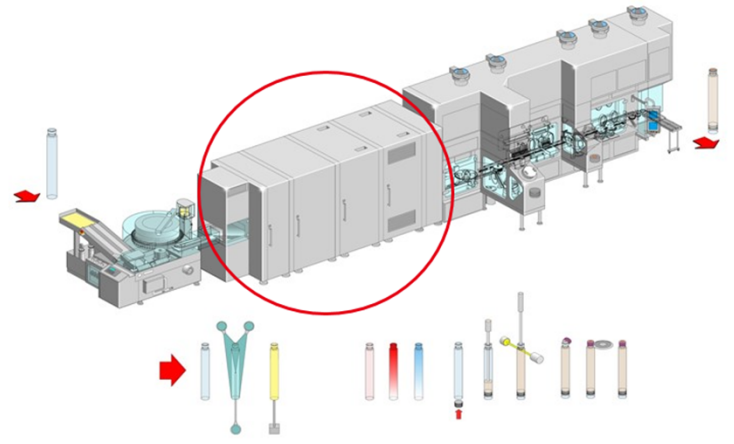
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Machine impact on containers

Critical areas – Sterilization Tunnel



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Machine impact on containers

Where is impact on the glass?



Cartridge processing,
Sterilizing tunnel.
Heating of glass containers
up to 300 degrees Celsius

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Critical areas – Sterilization Tunnel



- **Pressure** on Containers in Tunnel Infeed Section
- Heating of glass Containers up to **>300 degrees Celsius**
- **Direct Glass to Glass Contact** within the System
- **Stress** due to **Cool-Down** of Containers

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Sterilizing tunnel - Infeed / Discharge

- Accumulation control with bulk infeed, bulk transport and bulk discharge



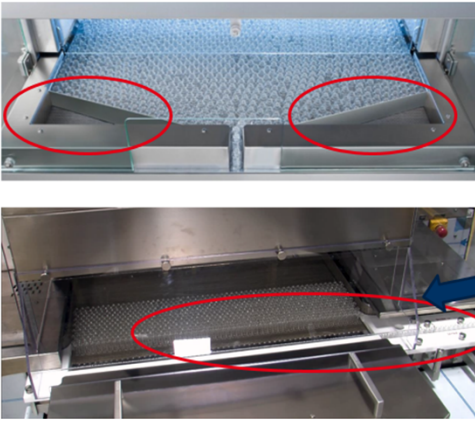
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Solutions – Sterilization Tunnel



- **Accumulation control** at infeed section
- **Pre-Heating Zone** to reduce temperature influence
- **Row by row loading:** Loading onto the belt with minimal contact between the containers
- **Three Belt System:** Main belt and side belts movement is synchronized

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Row by row transfer



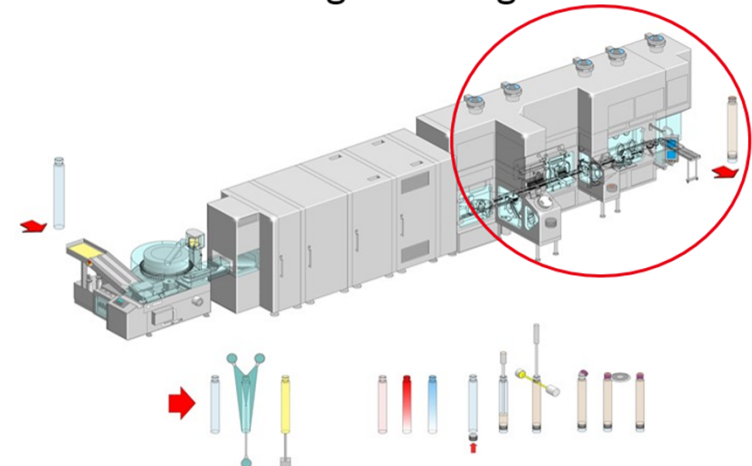
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Critical areas – Filling & Closing



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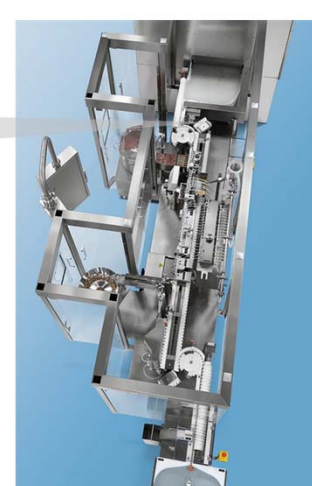
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Where is impact on the glass?

Where is neuralgic point:
Separation of glass containers
after sterilization



Cartridge processing


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Precision – Filling of cartridges



Cartridge for pen system
Hole for filling \varnothing (inner) = $3,15 \pm 0,2\text{mm}$

Filling needle \varnothing (outside) = 2 mm

Only 0,5 mm air gap!

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Solutions – Filling & Closing


Carrier System:

- **Precise and individual** transportation through the Filling and Closing Machine



Closing:

- Adjustable pressure and slight rolls
- Cartridge is rotated from both ends



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Machine impact on containers

And how can the impact be reduced?

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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

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And how can the impact be reduced?



Line without any
glass to glass contact


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Robotic feeding



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Machine impact on containers

Stainless steel transport pucks




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Washer outfeed/tunnel infeed - detail




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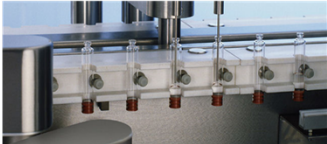
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Infeed filling machine with transport pucks



Special transport carriers




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Infeed with robotic systems and transport tray




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Machine impact on containers

Infeed with robotic systems and transport tray




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Machine impact on containers

Infeed filling machine with transport pucks




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Infeed filling machine with transport pucks




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Nested syringes




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Machine impact on containers

Nested syringes



Centering plate
stainless steel



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Nested syringes – alternative centering plate

Centering plate plastic material



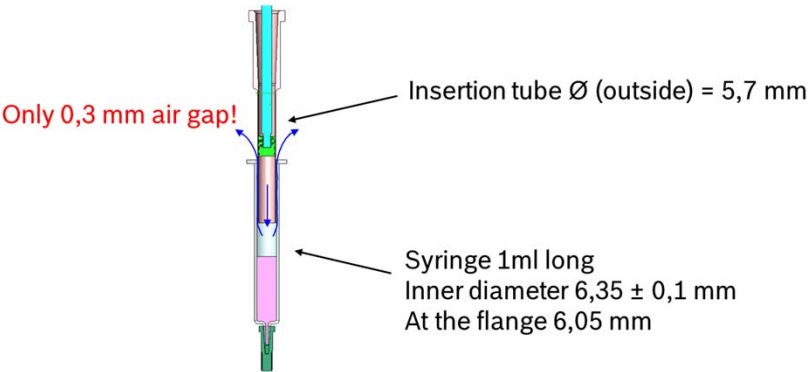
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Precision – Stoppering of syringes



Only 0,3 mm air gap!

Insertion tube \varnothing (outside) = 5,7 mm


Syringe 1ml long
Inner diameter $6,35 \pm 0,1$ mm
At the flange 6,05 mm

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Insertion tubes

Filling needles

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Special solution: Nested vials and cartridges




Photo: Schott, adaptiQ
Internet press news

Photo: Ompi, EZ fill

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Filling of nested vials



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Downstream – example denesting



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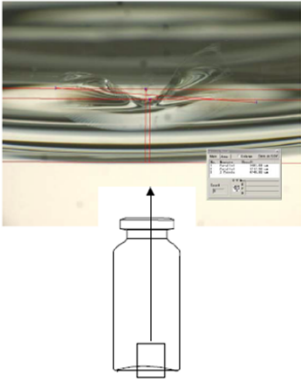
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Case study – vials damaged in bottom area

Analysis by customer



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

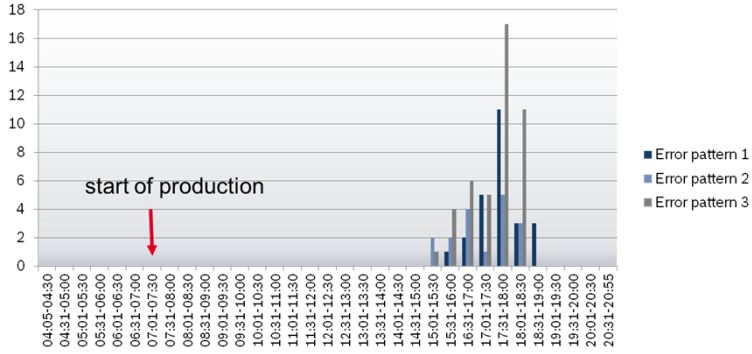
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Number of damages over time



| Date | Error pattern 1 | Error pattern 2 | Error pattern 3 |
|-------------|-----------------|-----------------|-----------------|
| 04-05-04:30 | 0 | 0 | 0 |
| 04-31-05:00 | 0 | 0 | 0 |
| 05-01-05:30 | 0 | 0 | 0 |
| 05-31-06:00 | 0 | 0 | 0 |
| 06-01-06:30 | 0 | 0 | 0 |
| 06-31-07:00 | 0 | 0 | 0 |
| 07-01-07:30 | 0 | 0 | 0 |
| 07-31-08:00 | 0 | 0 | 0 |
| 08-01-08:30 | 0 | 0 | 0 |
| 08-31-09:00 | 0 | 0 | 0 |
| 09-01-09:30 | 0 | 0 | 0 |
| 09-31-10:00 | 0 | 0 | 0 |
| 10-01-10:30 | 0 | 0 | 0 |
| 10-31-11:00 | 0 | 0 | 0 |
| 11-01-11:30 | 0 | 0 | 0 |
| 11-31-12:00 | 0 | 0 | 0 |
| 12-01-12:30 | 0 | 0 | 0 |
| 12-31-13:00 | 0 | 0 | 0 |
| 13-01-13:30 | 0 | 0 | 0 |
| 13-31-14:00 | 0 | 0 | 0 |
| 14-01-14:30 | 0 | 0 | 0 |
| 14-31-15:00 | 0 | 0 | 0 |
| 15-01-15:30 | 0 | 0 | 0 |
| 15-31-16:00 | 0 | 0 | 0 |
| 16-31-17:00 | 0 | 0 | 0 |
| 17-01-17:30 | 0 | 0 | 0 |
| 17-31-18:00 | 0 | 0 | 0 |
| 18-01-18:30 | 11 | 17 | 11 |
| 18-31-19:00 | 3 | 3 | 3 |
| 19-01-19:30 | 0 | 0 | 0 |
| 19-31-20:00 | 0 | 0 | 0 |
| 20-01-20:30 | 0 | 0 | 0 |
| 20-31-20:55 | 0 | 0 | 0 |

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Analysis by 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

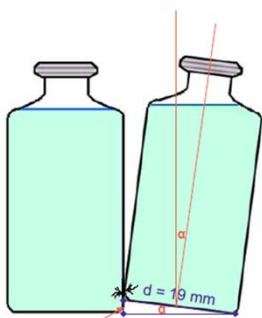
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Crash constellation



$\Delta E = 0,93 \text{ mm}$
 $\alpha = \arcsin(0,93/19) = 2,81^\circ$

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New sizepart at outfeed

Small change → huge effect

old contour

new contour

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Summary

- Technical solutions/concepts are available
- But there are limitations (costs, space...)
- New, other disadvantages could be created
- Optimization vs. new concepts

Where we should end up

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

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Questions?



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