

Implementation of a Laser-Assisted Cutting Technology in the Manufacturing Process of Pre-Filled Syringes (PFS)

Philippe Lauwers

Business Unit Director PFS

Nipro PharmaPackaging

Agenda

1. Nipro PharmaPackaging (NPP) Introduction
2. On the origin of particles
3. Bulk PFS conversion process – introduction of an innovative laser-based cutting (LBC) system
4. Study results: (sub-)visible particle load
5. PFS/AI integration-related challenges
6. Study results: Finger Flange thickness and strength
7. Benefits and Summary
8. Future Developments

1. Nipro PharmaPackaging (NPP) Introduction



Established
1954 Osaka Japan

Net sales
2.5 Billion EURO

Employees
23.200

Pharmaceutical

- Oral drugs
- Injectable drugs
- External drugs



Medical

- Dialyses products
- Injection products
- Catheter products
- Transfusion products



PharmaPackaging

- Glass tubing
- Glass packaging
- Plastic packaging
- Components & accessories



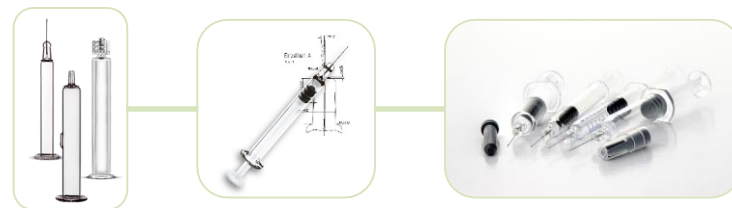
Long-term partner for Pre-Filled Syringes

Long-term experience in PFS development & production

Extended product portfolio

Standard

Customized solutions

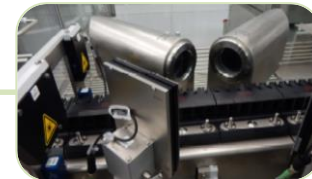
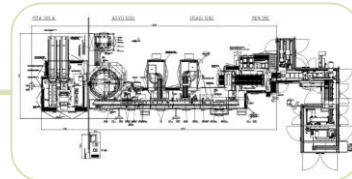


Strong future investment in PFS

Extension of plant

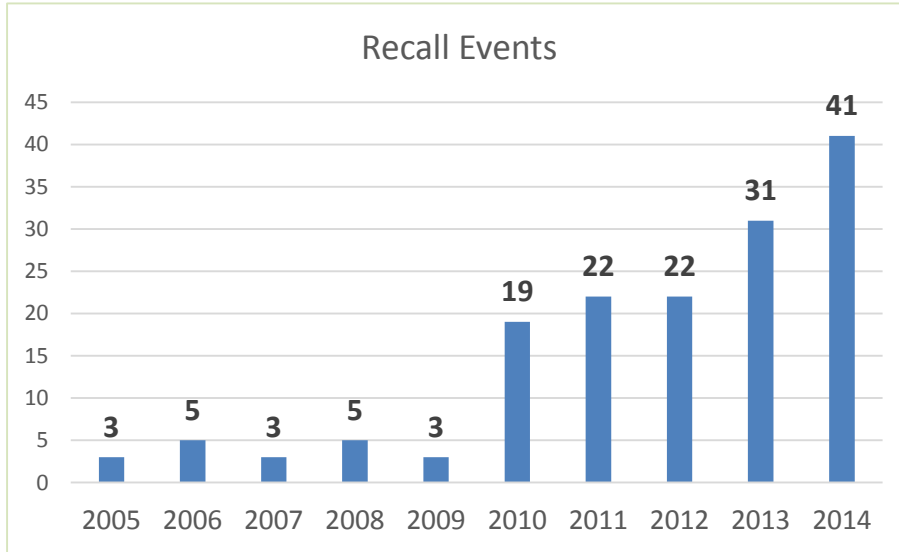
New manufacturing lines

Latest technologies

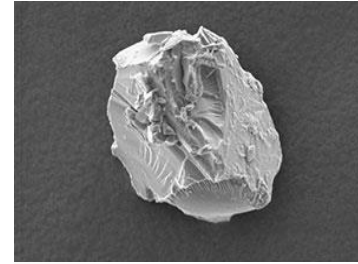


2. On the origin of particles

FDA reported 22 % recalls for sterile injectable drugs in period of 2008-2012 caused due to presence of visible particles



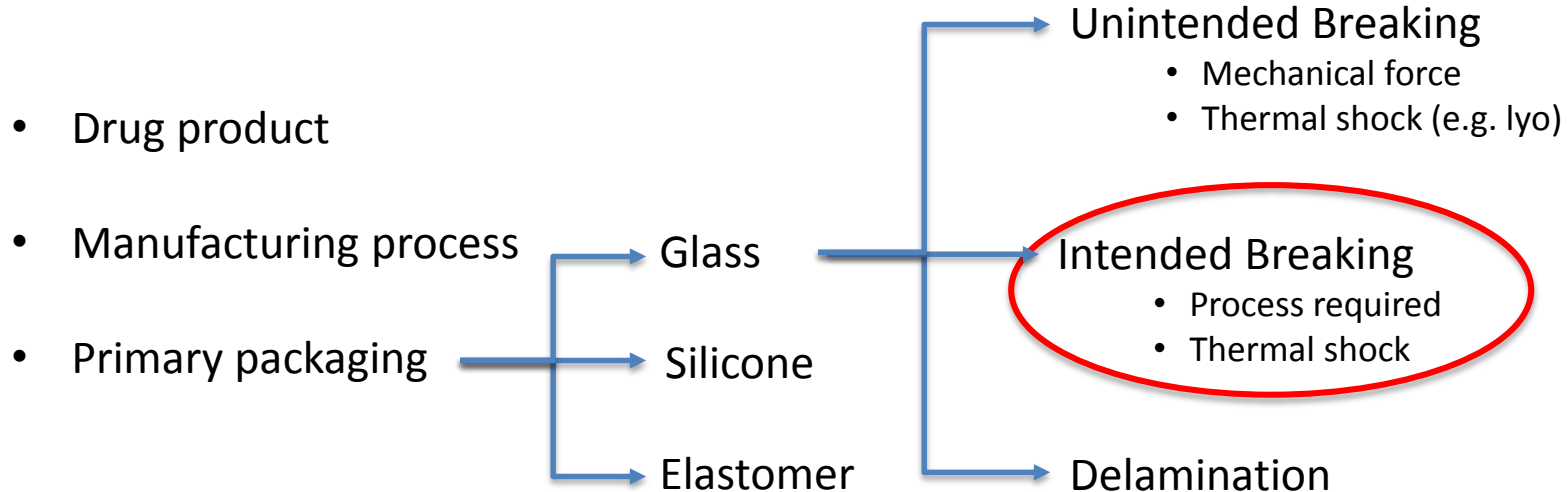
Source: Shabushnig JG (2014) Detection and Control of Visible Particles in injectable products.



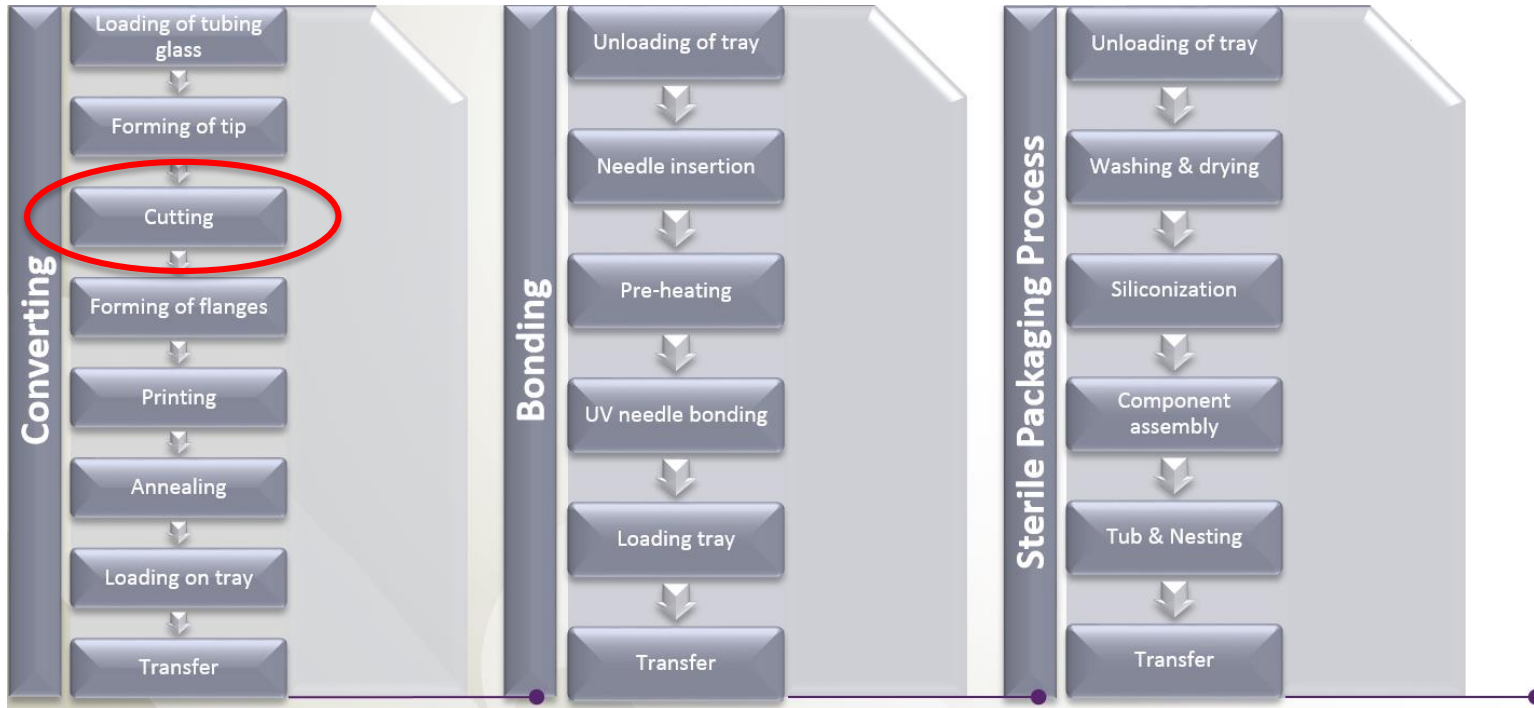
Since 2006, nearly 50 medications have had glass breakage or glass particulate issues serious enough for FDA recalls, impacting more than 100 million units of medication.* While the risk to human health is paramount, glass particulates contribute to other global healthcare issues like recalls and drug shortages.

*Source: US Food and Drug Administration. Enforcement Reports

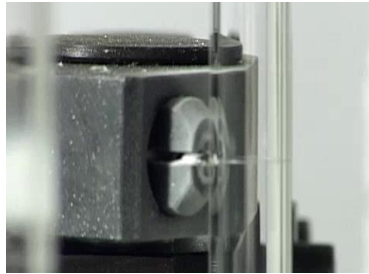
2. On the origin of particles



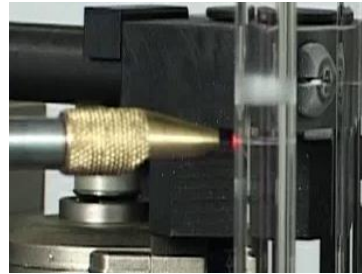
NPP's Pre-Filled Syringes Production Process



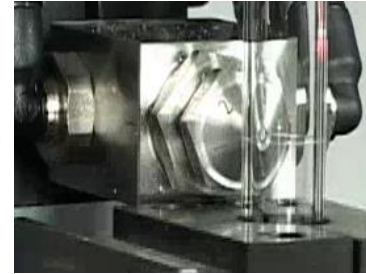
3. Bulk PFS conversion process - traditional bulk PFS cutting process



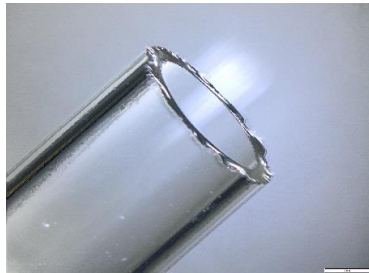
1. Scoring



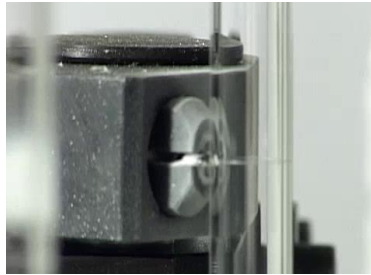
2. Heating



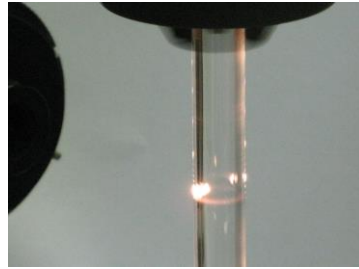
3. Water spray



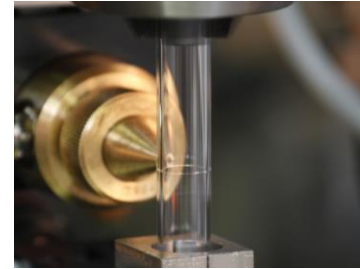
3. Bulk PFS conversion process – introduction of an innovative laser-based cutting (LBC) system



1. Scoring



2. PLC-controlled laser heating process



3. Water spray



4. Traditional bulk PFS cutting process vs. LBC

Methodology



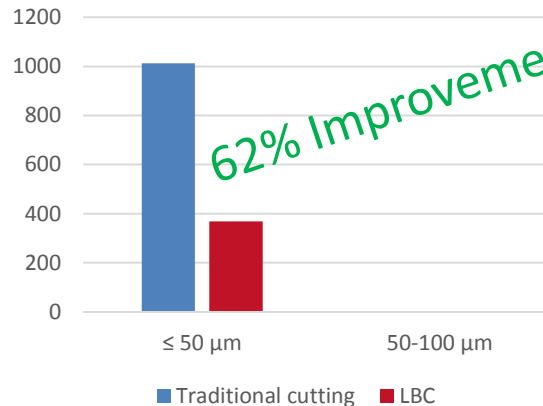
- 60 syringes from each sample lot rinsed with distilled water and sonicated
- Suspension filtered (0.2 µm mesh size)
- Microscopic particle counting

Results

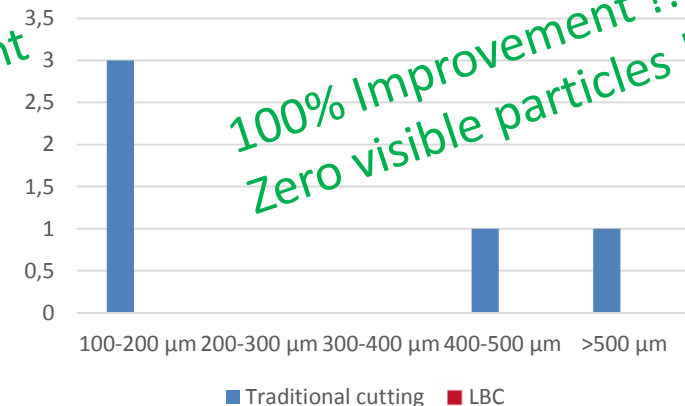


- Significant reduction of glass subvisible particles with N-LBC compared to traditional cutting
- No visible particles found with N-LBC

Glass Particles - subvisible range



Glass Particles - visible range



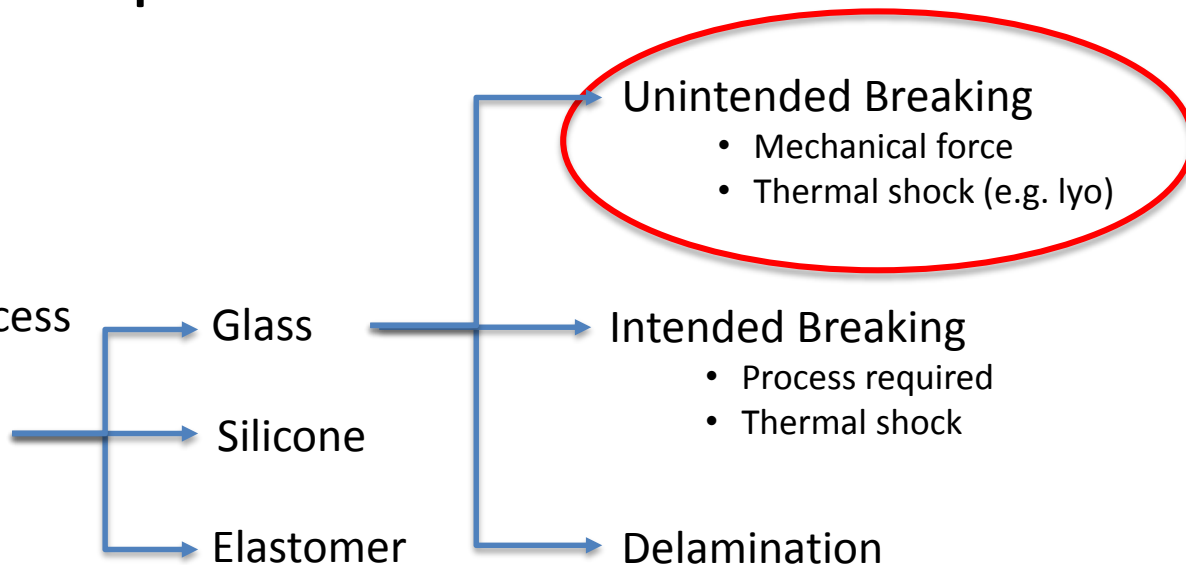
Study performed in collaboration with „Zentrum für Glas- und Umweltanalytik GmbH“
Centre for glass investigations and environmental analysis

On the origin of particles...

- Drug product

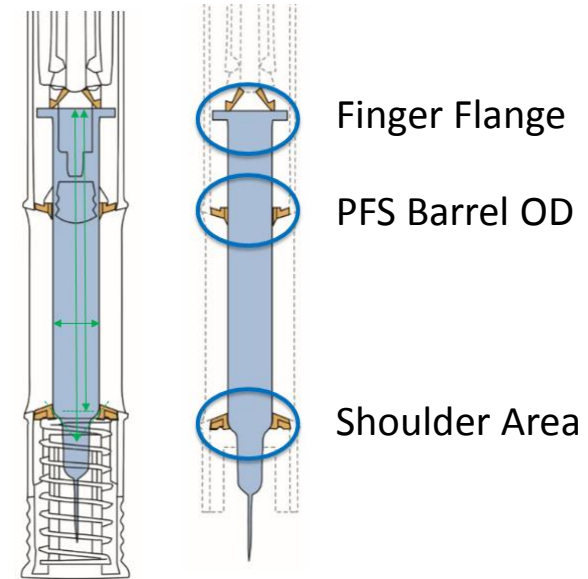
- Manufacturing process

- Primary packaging



5. PFS/AI integration-related challenges

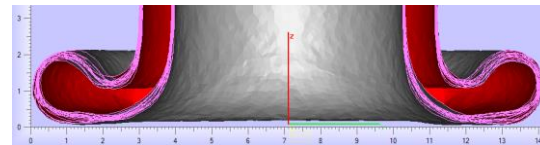
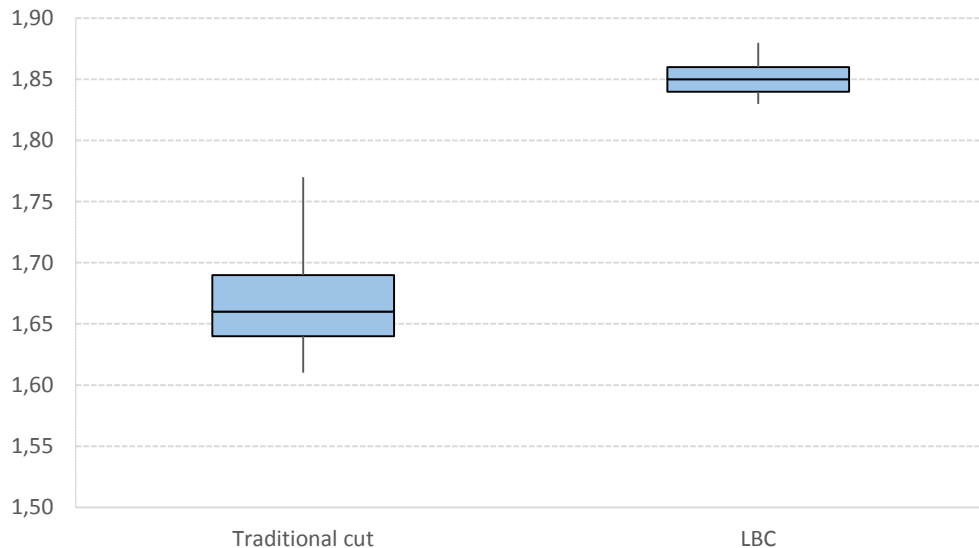
- Silicone distribution / profile accuracy
- Needle ID consistency
- PFS dimensional accuracy
- PFS mechanical properties
- Etc.



Courtesy of SHL

6. Study results: FF thickness

Finger Flange Thickness (mm) - 1ml Long Syringe



ISO 11040-4: 1.9mm +/- 0.5

Nipro: nominal +/- 0.25

80 bulk PFS tested per cutting method

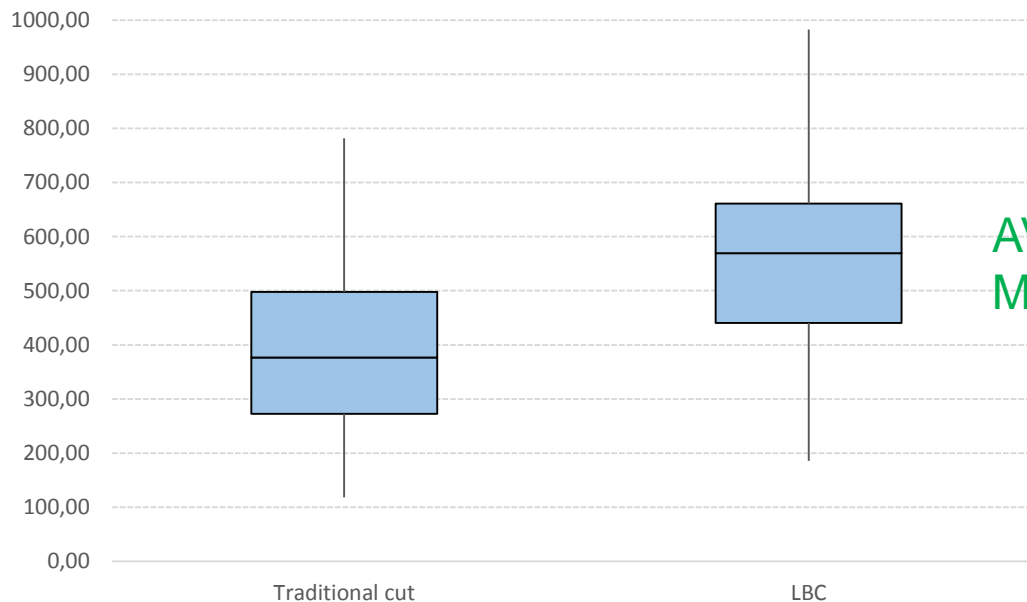
6. Study results: FF strength

Methodology



- 80 syringes tested for each sample lot
- Test speed 25mm/min
- Internal limit 35N

Finger Flange Strenght (N) - 1ml Long Syringe



AVG + 40%
MIN + 57%

7. Benefits and Summary

PharmaCos



Improved TCO through:

- Less glass particles which mitigate risk of rejections at fill & finish site
- Lower risk of finger flange breakages during F&F operations
- Lower risk of market recalls due to glass particulates or device functional failures

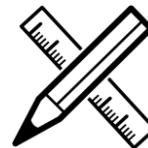
Patients



Enhanced patient safety

- Lower risk of glass particles inside PFS
- Safer drug delivery devices

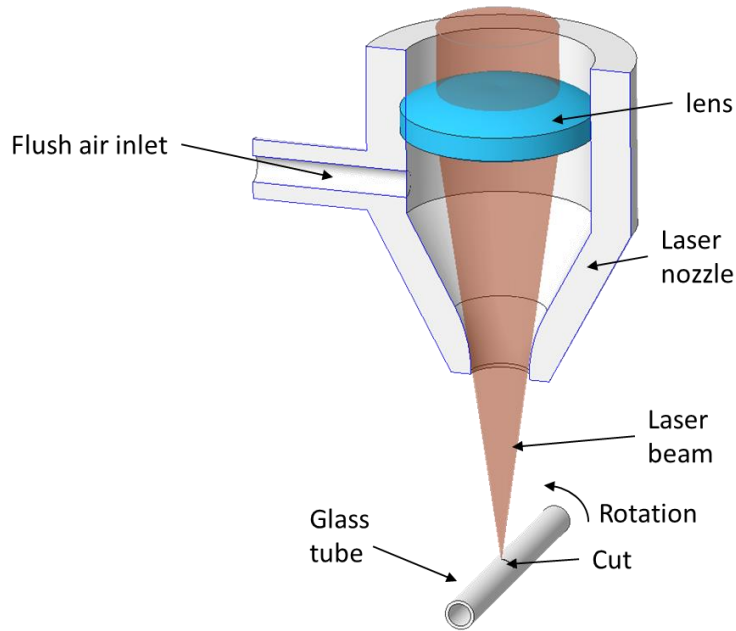
AI developers



- More reliable and **optimized integration between AIs and PFSs**
- Smoother assembly operations

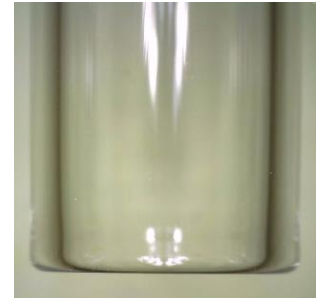
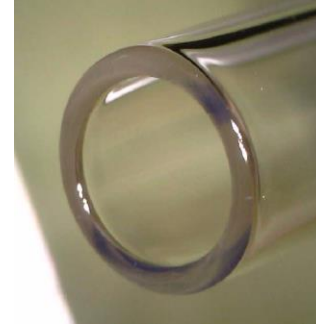
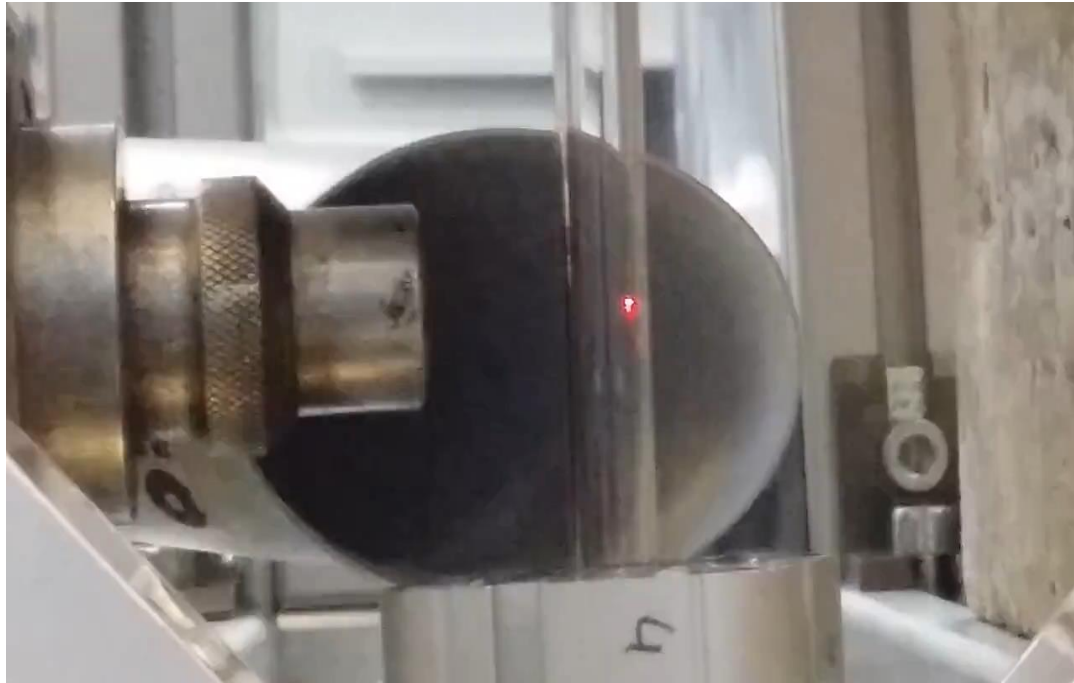


8. Future development: Advanced Laser Sublimate Cut



- To avoid any glass particle being generated during cutting
- To enhance cut length precision and perpendicularity
- To maximize opening for filling (cartridges)
- To improve overall cut quality

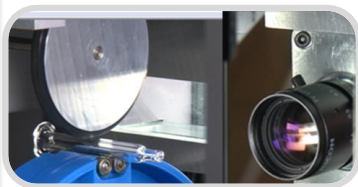
8. Future development: Full Laser Cut



Next generation laser cutting, making intended breaking obsolete...



- Laser Based Cut (LBC)



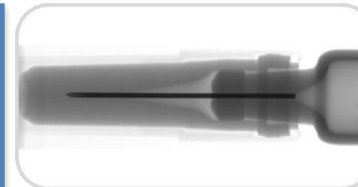
- Inline and real time camera inspection for dimensional and cosmetic aspects



- Maximum Automation
- Free of any glass to glass contact
- Glass to metal reduced to the absolute minimum



- Inline and real time camera inspection for silicone oil distribution



- Inline and real time X-ray camera inspection for needle & needle shield integrity

Acknowledgments

Nipro PharmaPackaging Germany:

Alfred Breunig, Udo Rossmann, Klaus Wuttke, Michael Thiel,
Roland Heller, Udo Schwarz, Michael Drössler, Martina Nachtigall,
Massimo Imberti

Zentrum für Glas- und Umweltanalytik GmbH:

Markus Daniel, Martin Witscher

Matteo Falgari

Patrick Grüninger

Thank you for your attention !

