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

**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

Established 1954 Osaka Japan  
Net sales 2.5 Billion EURO  
Employees 23,200
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.

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

- Drug product
- Manufacturing process
- Primary packaging

Unintended Breaking
- Mechanical force
- Thermal shock (e.g. lyo)

Intended Breaking
- Process required
- Thermal shock

Delamination

Glass
Silicone
Elastomer
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

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

\[ \begin{align*}
\text{Glass} & \quad \text{Elastomer} \\
\text{Silicone} & \quad \text{Delamination}
\end{align*} \]

**Unintended Breaking**
- Mechanical force
- Thermal shock (e.g. lyo)

**Intended Breaking**
- Process required
- Thermal shock

---

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

Universe of Pre-filled Syringes & Injection Devices | October 17-18, 2016 | Hyatt Regency Huntington Beach Resort and Spa | Huntington Beach, CA
5. PFS/Al integration-related challenges

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

Courtesy of SHL

Finger Flange
PFS Barrel OD
Shoulder Area
6. Study results: FF thickness

Finger Flange Thickness (mm) - 1ml Long Syringe

80 bulk PFS tested per cutting method

ISO 11040-4: 1.9mm +/- 0.5

Nipro: nominal +/- 0.25
6. Study results: FF strength

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

---

**Finger Flange Strength (N) - 1ml Long Syringe**

- **Traditional cut**
  - AVG + 40%
  - MIN + 57%

- **LBC**

---

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

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

Enhanced patient safety

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

• 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!