Connecting People, Science and Regulation

Functional integration of PFS into autoinjector: components selection and performances characterization

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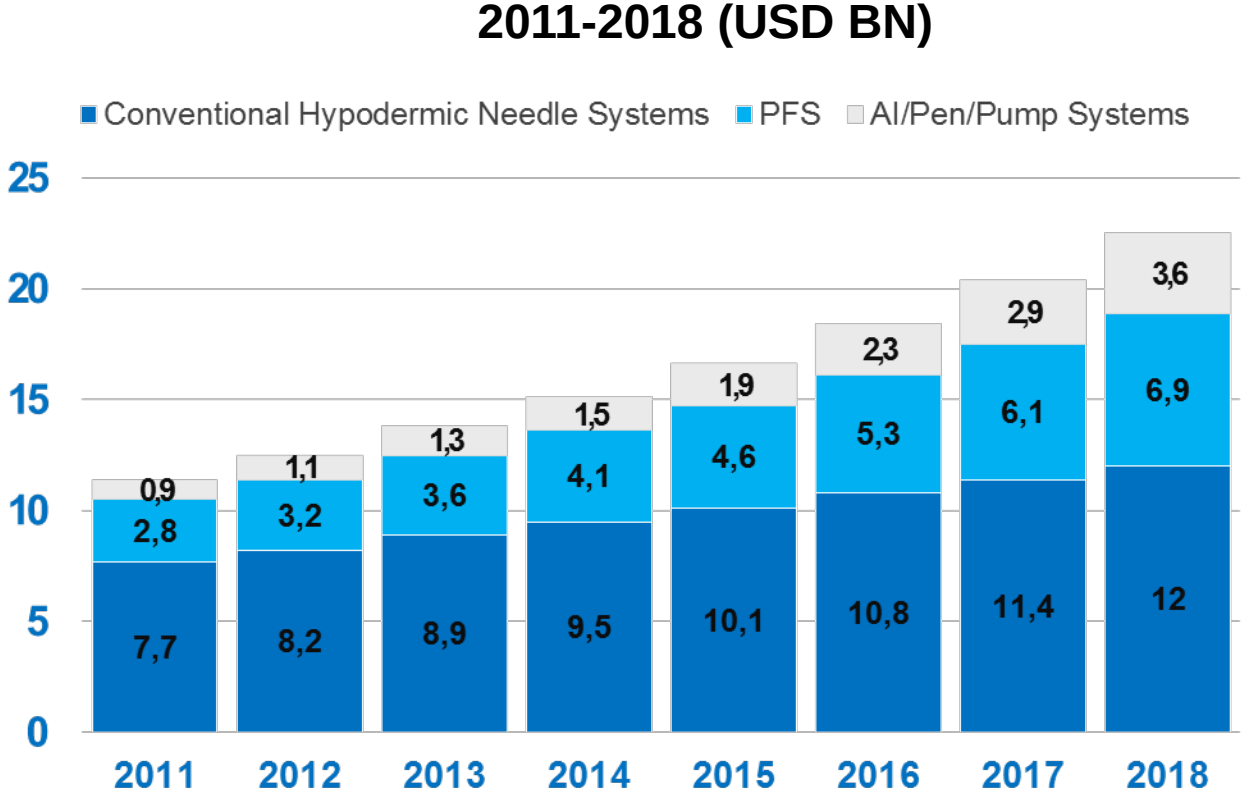
Outline

- Market trend
- PFS and AI
- RNS vs FNS
- Silicone treatment characterization

Market trend



CAGR 2012-18 (%)

23%

14%

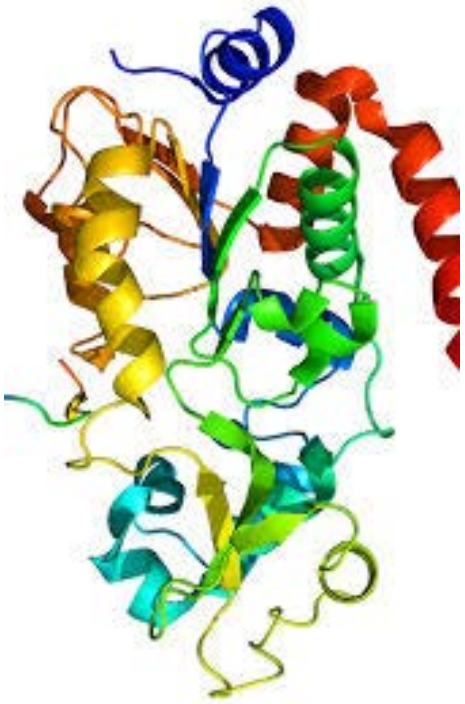
6,5%

RELATED PRIMARY CONTAINER

Source: Roots Analysis 2013

Market trend

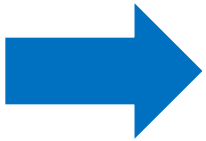
- More generics & biosimilars are coming as patents expire and this has the potential to further expand the market
- Devices are seeing as a possible solution for the differentiation
- Device to ease the patient with chronic disease



Benefit for patients

- Devices can help to overcome fears of needles
- Devices as a prevention for needle stick injuries
- Devices can make the injection process simple & more intuitive

PFS and AI

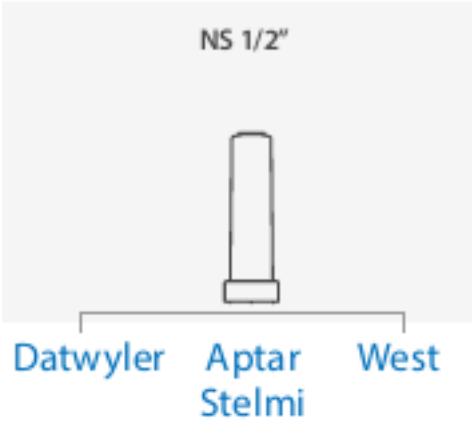


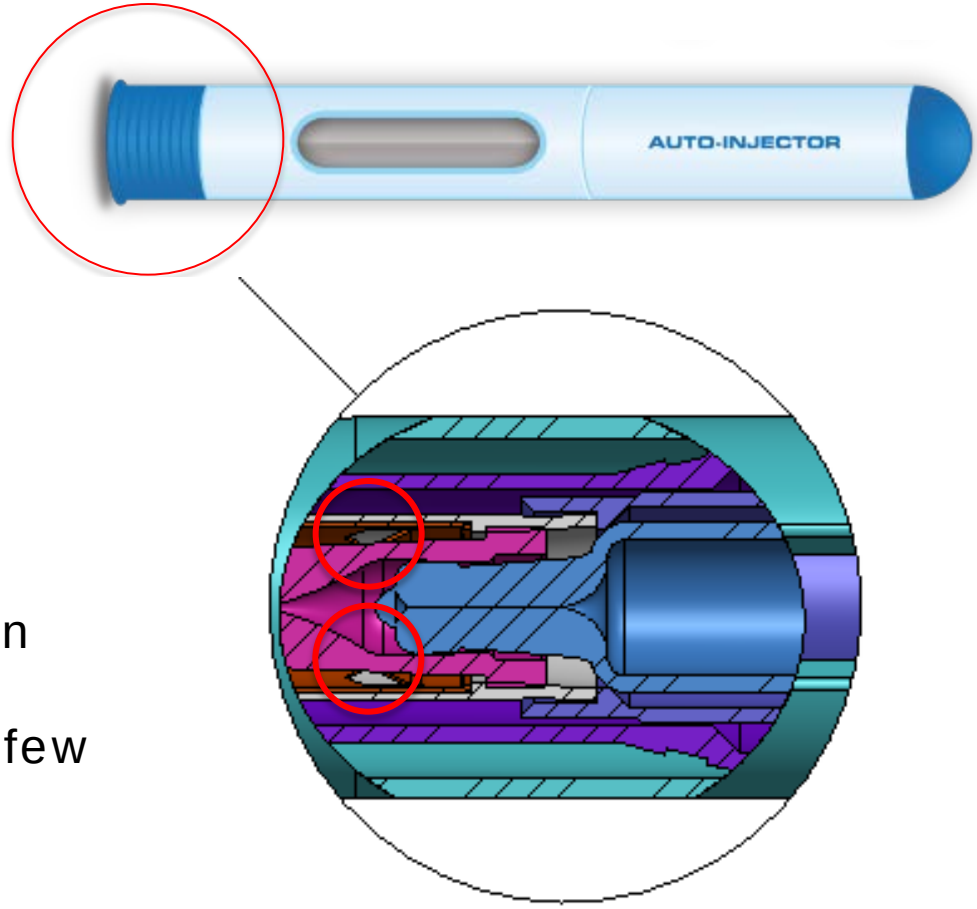
RNS

?

FNS

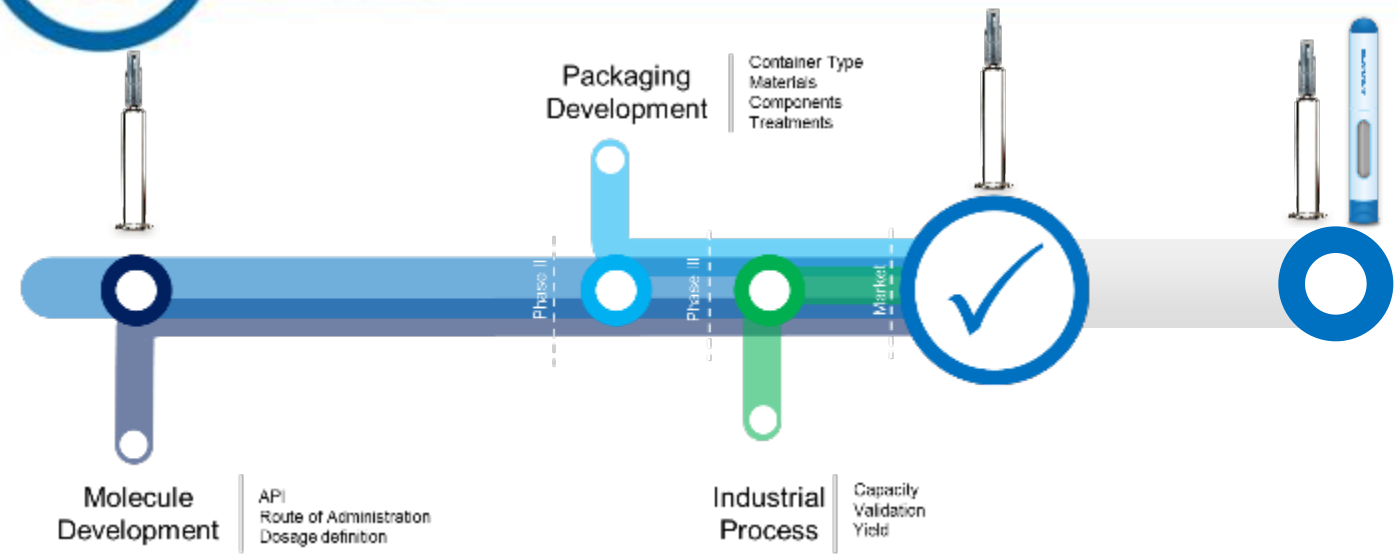
Needle shield and AI Cap



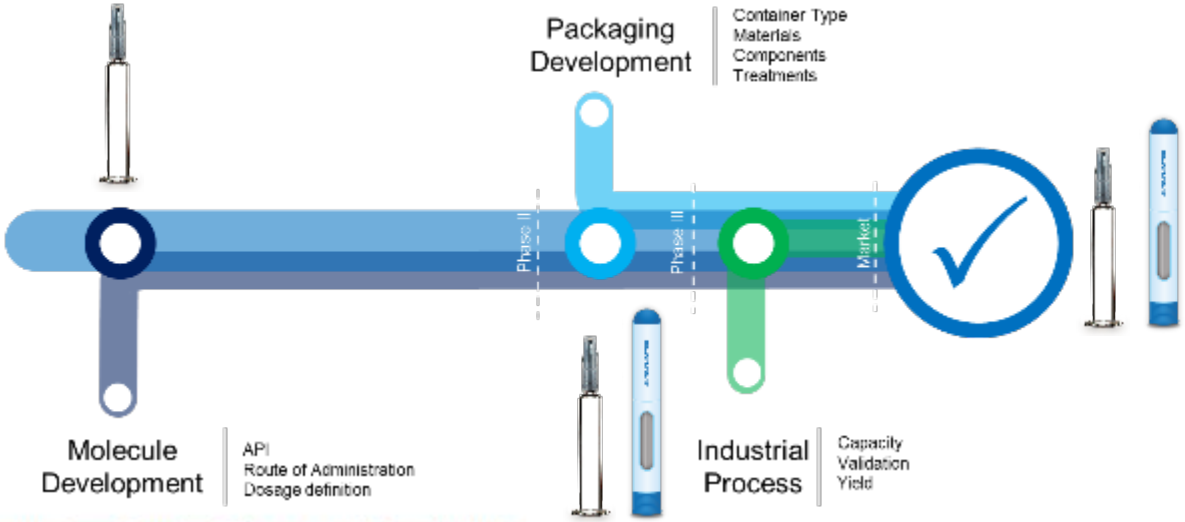


The AI cap has some FNS grabbing features that are in general able to manage different FNS (or requiring a few adaptations)

PFS and AI



Before:
Complement of the PFS



Today:
AI introduced in early stage

FNS vs RNS: some considerations

- The RNS dimensions and designs are complicating the connection with the RNS Grabber/Decaper

- RNS, because of the robustness, needle pricking and safe handling, is used for manual injections

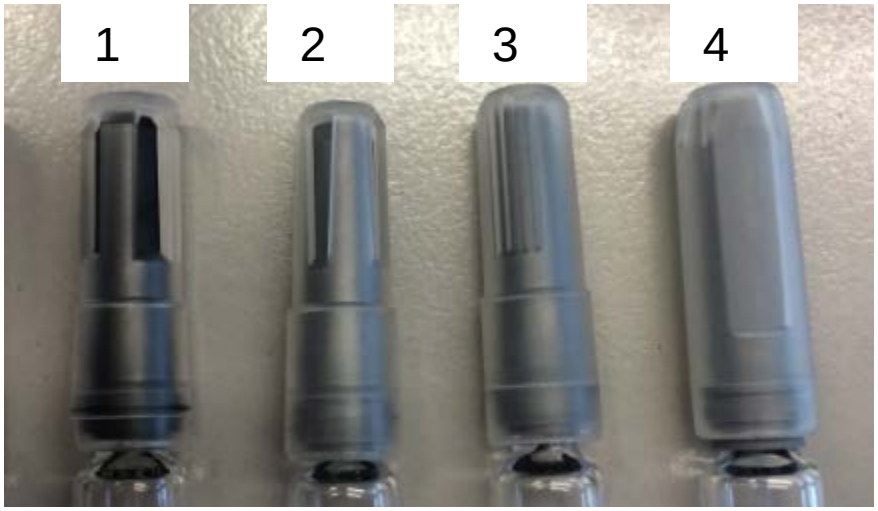
- The introduction of the AI in early stage is leading the customers to think about only one syringe format for the future syringe platforms based on RNS

- Customers potentially want to have more than one interchangeable syringe supplier
  - Same dimensional characteristic of the barrel
  - Same rubber components and RNS
  - Same functional performances

RNS: some considerations

This is even more complicate because the RNS in the market have different shapes and dimensions

www.bd.com



1. Aptar P0237 (Stelmi – special autoinjector RNS)
2. Aptar P0037 (Stelmi – standard RNS)
3. Datwyler P8567B
4. West 4144

Courtesy of Aptar-Stelmi, Datwyler and West

Courtesy of Terumo

FNS vs RNS: open points

Scenario 1:

- RNS free/ISO std shape supplied by the different closures suppliers
  - Increase the compatibility between the different rubber options
  - Reduce the time for PFS integration into AI
  - Establish std AI platform at the suppliers side

Scenario 2:

- Std pre-configured AI platform owned by the device suppliers to be customized
  - Available solutions for the different RNS options
  - Reduce the time for PFS integration into AI
  - Facilitate/Convince/Increase the interested on the AI solutions

Scenario ….

There is not only one option but the common message is increase flexibility, functionality and performances

Example of AI FNS/RNS compatible

KEY PRODUCT FEATURES:

- Ultra-Compact Design
- Simple 2-step Operation
- Integrated Safety Features
- Audible, visual and tactile feedback
- One-Handed Operation
- Versions for both FNS and RNS

BUSINESS MODEL:

- Minimized Investment Upfront
- Maximized Speed to Market

SHL GROUP

info@shl-group.com
www.shl-group.com

Courtesy of SHL

Example of AI FNS/RNS compatible

Device specifications

Primary container	1 ml long ½" PFS
Fill volume	0.2–1.0 ml
Dosing	Fixed, full content
Viscosity	1–35 cP
Injection time	< 10 s

Needle diameter	29G TW and larger
PFS needle shield	Rigid or soft
Needle insertion depth	5–8 mm
End of injection feedback	Audible and visual
Weight	35 g incl. glass PFS

The Ypsomate can manage the different RNS options and potentially the switch from FNS to RNS with some adaptations and of course Regulatory activities.

Courtesy of Ypsomed AG

Example of AI FNS/RNS compatible

The Bespak Syrina range of compact novel AutoInjectors has design options for both RNS and FNS

DEVICE SPECS	
Primary Container	1ml long, 1ml std – 3 ml (including 2.25 ml)
Fill Volume	Variable (delivers entire contents of syringe)
Viscosity limit	> 50 cP
Injection Time	Tuneable to 10 sec target
PFS Needle Shield	Options for RNS or FNS
User Feedback	Visual and audible

Syrina S 2.25 ml

BESPAK
A Consort Medical Company

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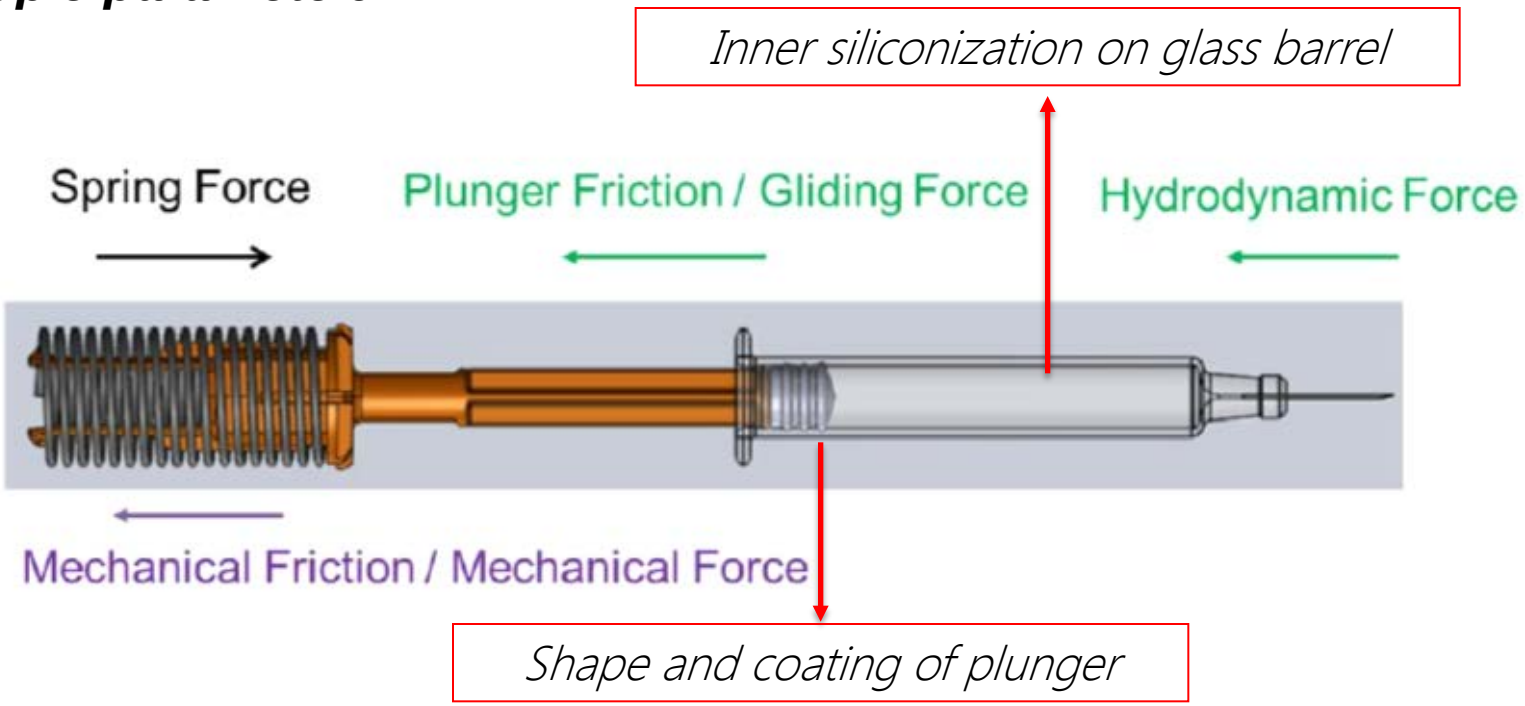
Courtesy of Bespak

Silicone treatment characterization

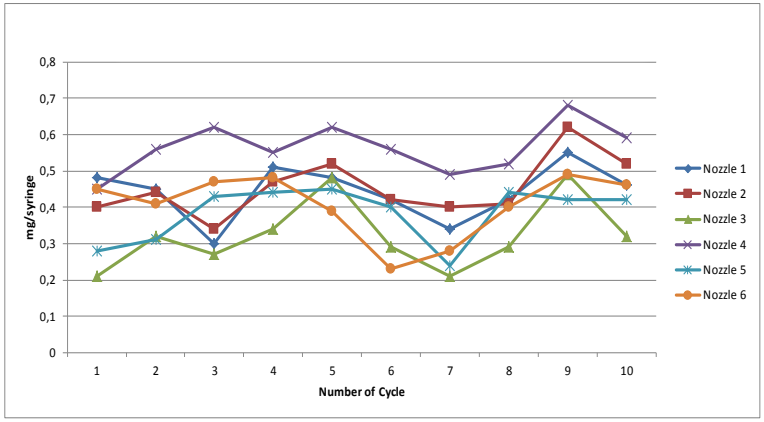
Autoinjector mediated drug delivery is a complex phenomenon, involving multiple parameters.



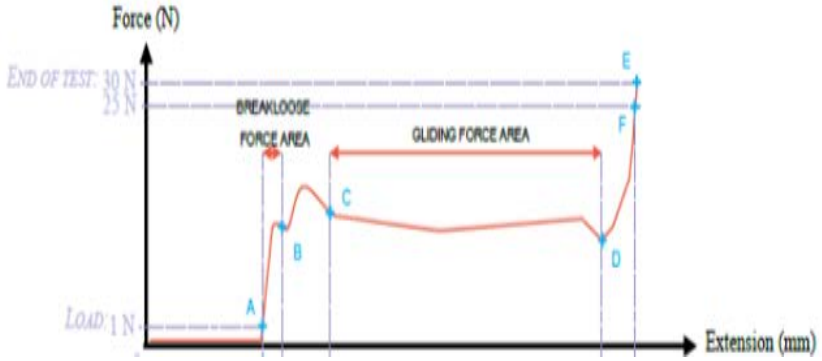
In this system the power unit provides a constant motion but not a constant force, having a uniform silicone coverage is a fundamental requirement on the final product. This can help maintaining a reliable maximum injection time over product shelf-life.

Silicone treatment characterization: the starting point

What kind of instruments should be used to deeper characterize silicone distribution?



Weight Test on single syringe, to determine cycle to cycle difference

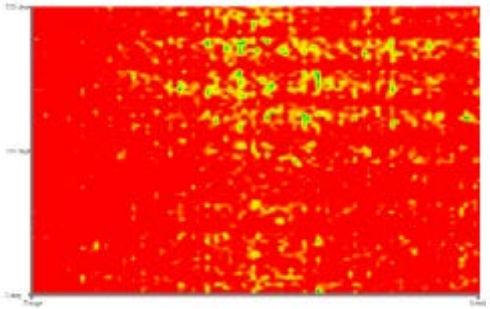


Glide Force with different speed to measure product performances with empty and filled containers.

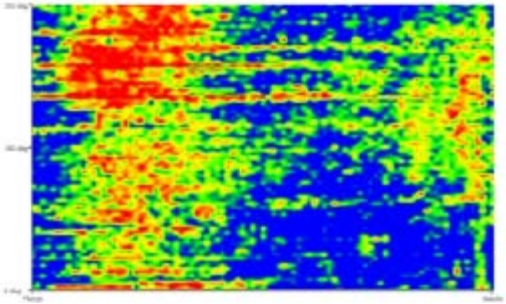
Standard Instruments

Silicone treatment characterization: other options

Nice to have instruments became a must for deeper detail on silicone distribution

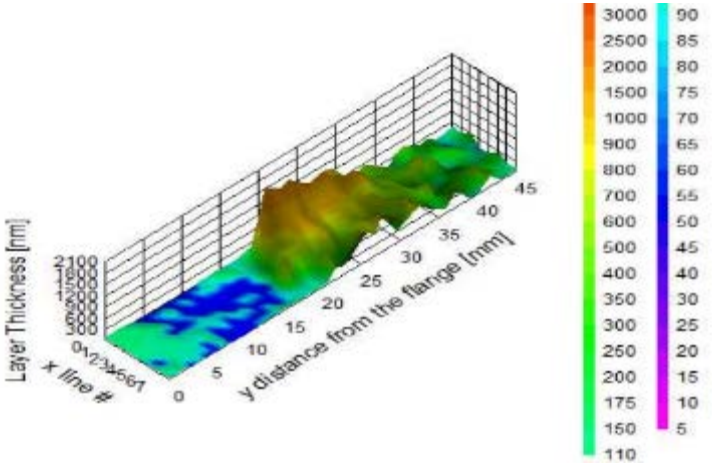


Good Coverage. Red = 100% coverage



Bad Coverage. Blue = Lack of silicone (Dry spots)

Heat Map with ZebraSci instrument to detect silicone coverage



Rap-Id technique to determine silicone thickness on the barrel

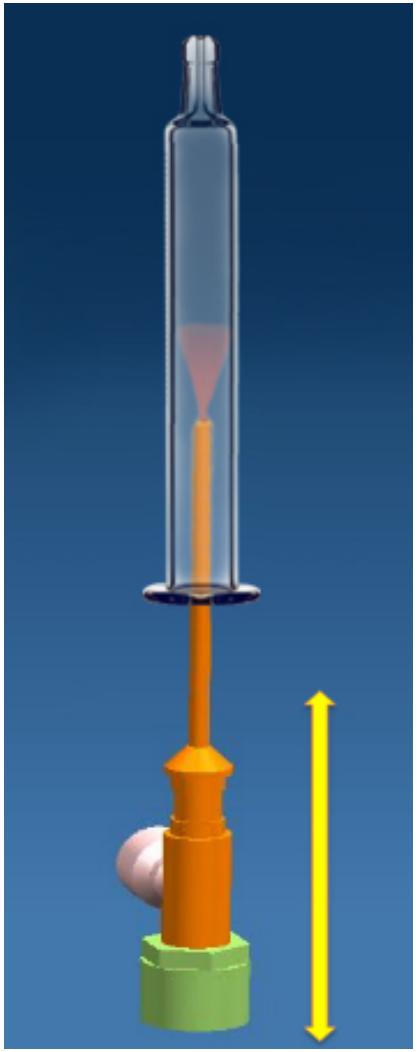
Silicone treatment characterization

- Over years silicone spraying technology moved from fixed nozzle to diving nozzle
- This technology is well known as state of the art for suitability on spraying tailored silicone quantity and distribution with high level of repeatability
- Ompi has evaluate different trials in order to explore best process capability available

Silicone treatment characterization

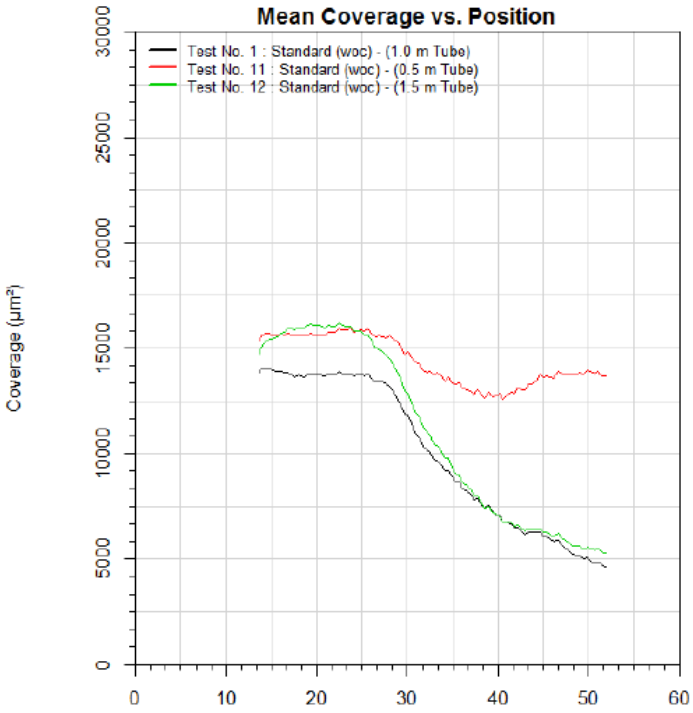
Which parameters can influence silicone distribution and barrel performances?

- Silicone tank pressure
- Tubing length between silicone pump and nozzle
- Nozzle Movement
- Silicone quantity
- Air atomization pressure
- Nozzle design



Silicone treatment characterization

Case study – how tubing Length can influence silicone distribution



Experiment:

On a table top unit siliconize syringes with three different tubing length:

Test no.1 = 1.0 m Tube

Test no.11 = 0.5 m Tube

Test no.12 = 1.5 m Tube

Silicone treatment characterization

Case study – how tubing Length can influence silicone distribution

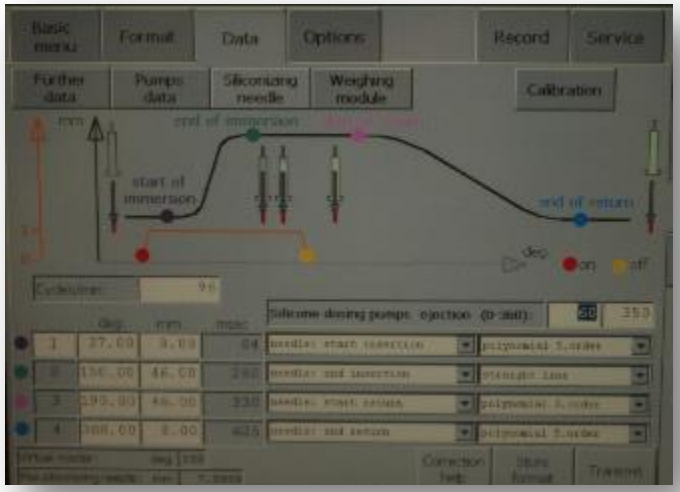
Shorter tube (50% less than standard between pump and nozzle) shows a more uniform coverage than other trials.

- The more “rigid” behavior of the tube
- Shorter time for the pressure cascade which passing the tube from the begin to the end of its length over injection time

Silicone treatment characterization

For having a robust silicone spraying process we have to ensure a robust process capability with state of the art solution such as:

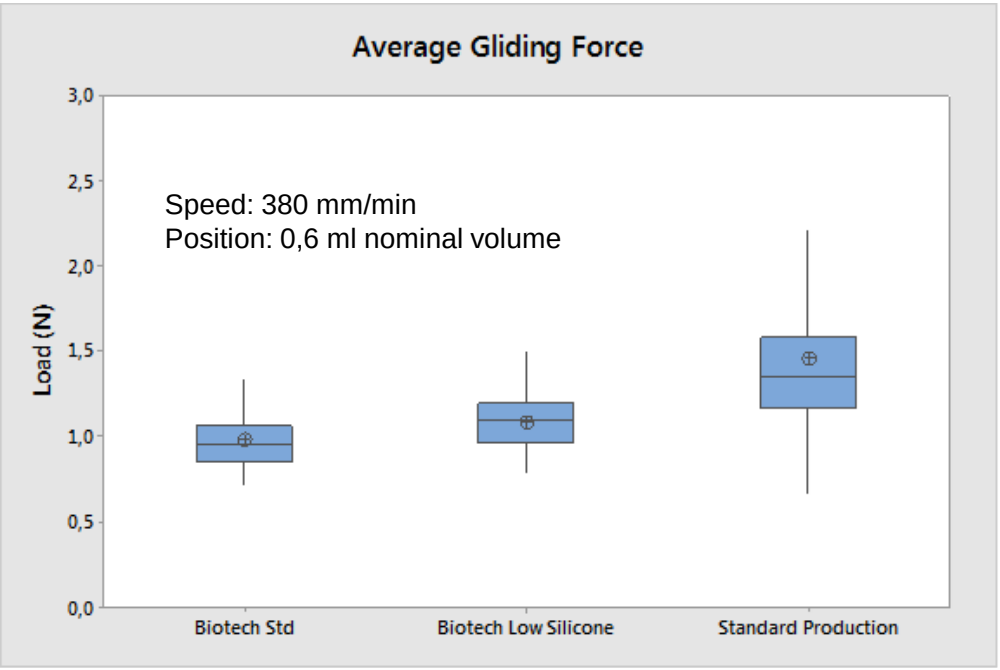
- HMI set-up of pumps vs manual setting: high accuracy of silicone dosing quantity
- 100% in line inspection of silicone distribution vs IPC: can detect both differences on silicone quantity and distribution
- Tailored Recipes for targeting desired silicone distribution



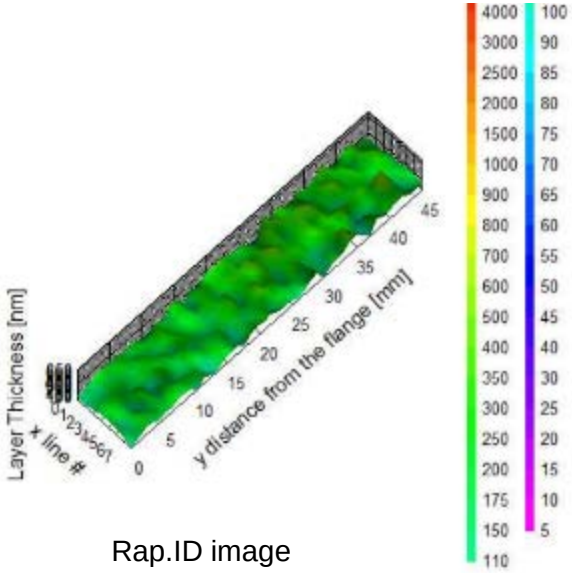
Silicone treatment characterization

In particular, achieving a uniform distribution is the key parameter for maintaining stable gliding performances.

Ompi is developing first trials of low silicone quantity (0,3 mg) for particular application



Injection time



Rap.ID image

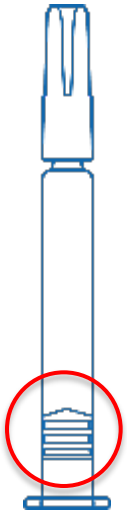
Siliconization for Biotech presents ideal characteristics for AI performances; standard production is indicated for manual injection

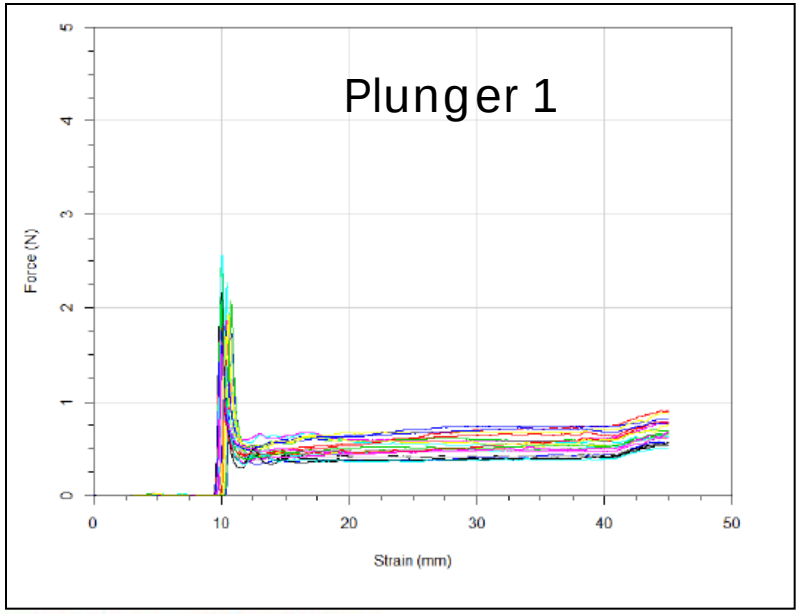
Silicone treatment characterization: rubber plunger

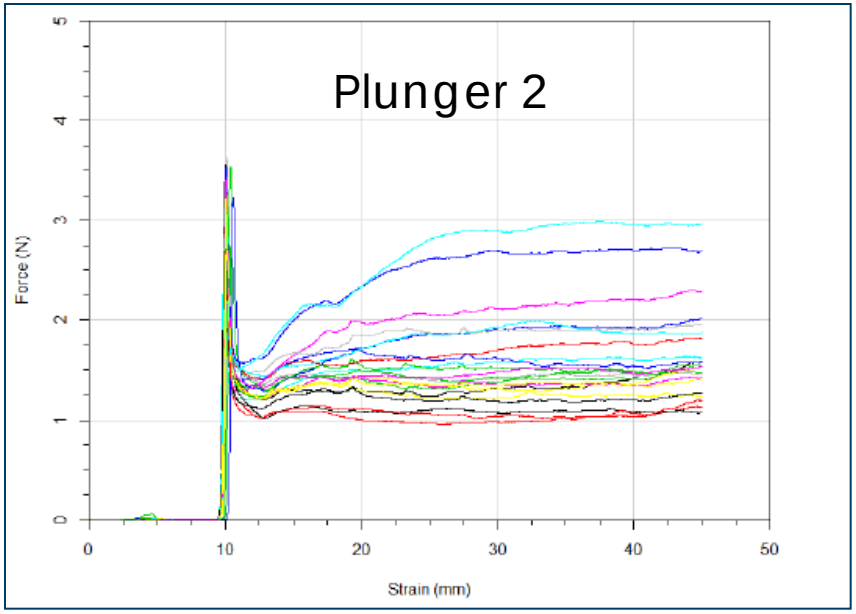
Even if with a good siliconization distribution, it is fundamental to choose the right plunger. In fact, due to the shape and coating of the plunger, performances can change drastically

- Barrel with same uniform silicone distribution
- Plunger with same rubber formulation
- Differences on shape and coating

With worst case gliding can be 4x higher than optimized solution!







Conclusion

- AI market is growing
- Flexibility is becoming always more relevant
- Components selection can effect performances
  - FNS/RNS is key for the AI platform selection
  - Rubber Stoppers design and formulation
- Functional characterization of the system is a must
- AI Design, Development and Integration are requiring joint efforts
- We are open to cooperate for further analysis with all partners

Acknowledgements

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Thank you for your attention

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