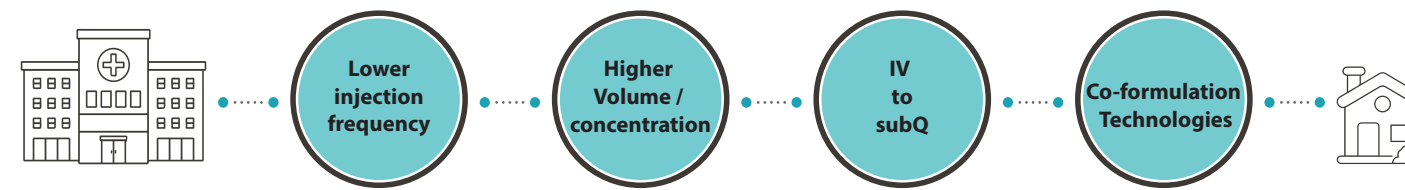


NeoFlex™ Worldwide: How Datwyler's Innovative Plunger Portfolio Addresses the Latest Trends in Drug Delivery

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Compatibility (E&L Profile)

NeoFlex™ Plungers (E&L – simulation study)

Samples:

- FM257 ('classic halobutyl')
- FM457 ('low extractables compound')
- NeoFlex = coated FM457
- Coated competition sample

Medium

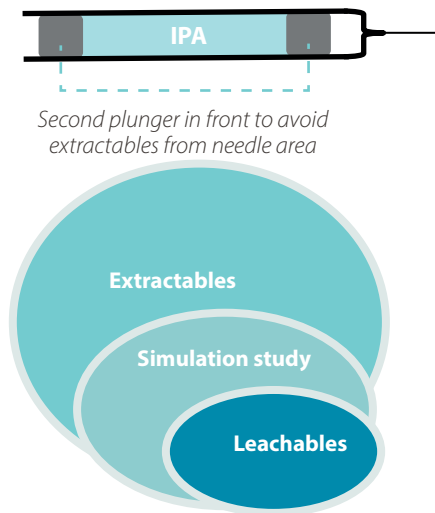
IPA

Extraction conditions

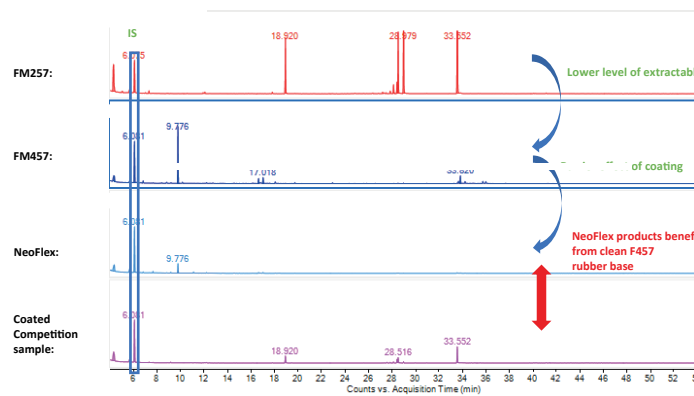
1 year storage with contact, at room temperature

Analysis

Analysis of the IPA using HS-GC/MS



Results HS-GC/MS (Volatile Organic Compounds)

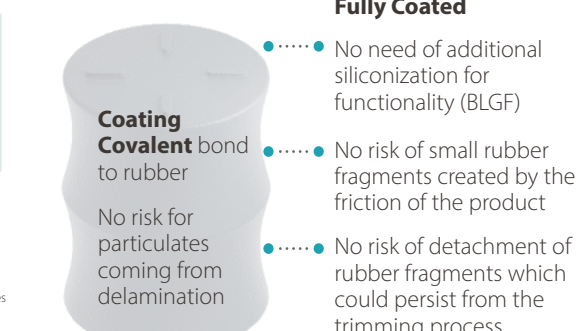


Minimizing Particulate Contamination

Process Particulates



Product Particulates



Particulate and silicone droplets can be critical for sensitive molecules and proteins, increasing the risk of interaction/aggregation

Proven Machinability

For coated plungers the insertion station is one of the most critical step

NeoFlex™ plungers are proven to optimally perform on vacuum assisted filling lines and, with some precautions, also with vent tube systems

The siliconized versions of the NeoFlex™ plungers make them suitable for vent tube F&F lines.

The additional siliconization on top of the fluoropolymer coating reduce the plunger friction in the non-lubricated steel tube during the insertion, so limiting the temperature increase.

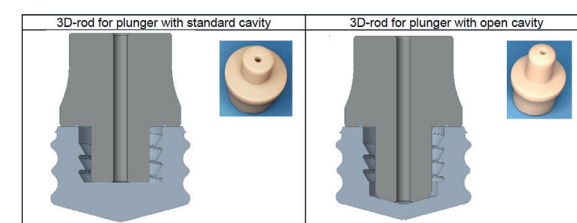
NeoFlex™, thanks to a thinner and more flexible coating, once siliconized, can work with vent tube placement, without the risk of wrinkles of the (thicker) film coated solutions

For high-speed lines, a short and polished vent tube also helps to limit the friction and temperature increase that can damage the coating and create particles, putting at risk the safety and functionality of the system.

Design/Functionality

10ml V9555 NeoFlex™ PFS Plunger:

The back cavity

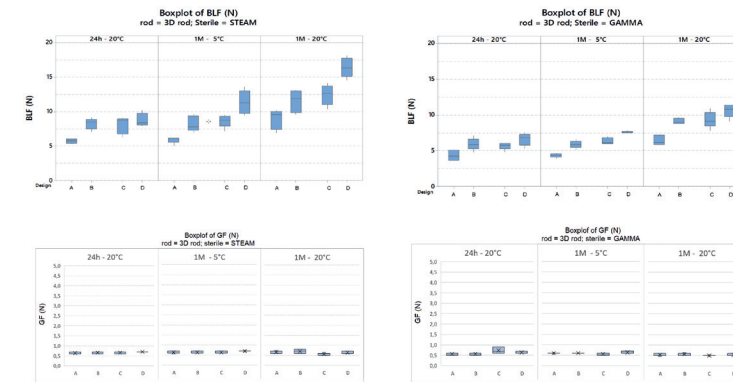


This cavity is the point of mechanical interface with the autoinjector

BLGF

NeoFlex™4 different designs (A,B,C,D) were tested for BLGF, also in combination with different sterilization methods.

Conditions: empty representative syringes, stored with empty back cavity, activation with non-threaded rod, speed 100mm/min

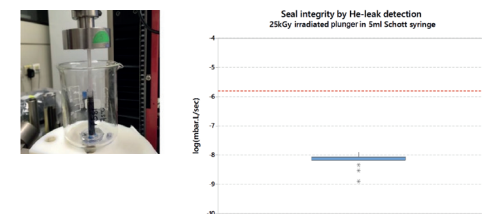


Design A (then V9555), showed the best results for BLF, so it was selected to proceed to the evaluation of the CCI

Plunger barrel seal integrity

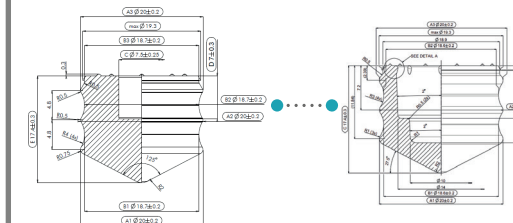
For the PBSI two methods were considered:

- The Blue dye test method Results: the seal integrity of 10 NeoFlex™ plungers (selected design and sterilization) in 5ml syringes is tested after 24h at room temperature. The seal integrity after compression (52N) is good: no leakages observed (n=10).
- He-leak detection method The seal integrity of 20 NeoFlex™ coated plungers (selected design and sterilization) in 5.5 ml syringes were good: all He-leak rates are consistent and below the Kirsch Criterion



10ml V9547 NeoFlex™ Cartridge Plunger:

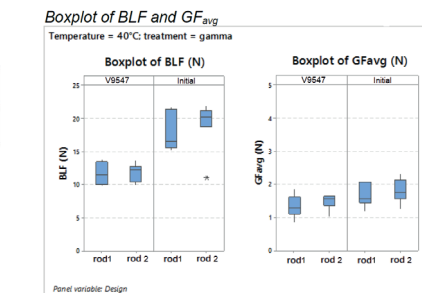
Optimization of functionality



Functionality of initial design 10ml wearable plungers was evaluated. Seal integrity was good, but gliding not in line with the expectation: the BLF of the nominal and maximal design plungers were far too high after 1 month storage (even >20N in the most severe storage condition).

Therefore a re-design project started with the target of improving the gliding behaviour, without putting at risk the seal integrity (He-leak). Different new designs were evaluated, with different inner cavities, rills geometry and total height

BLGF



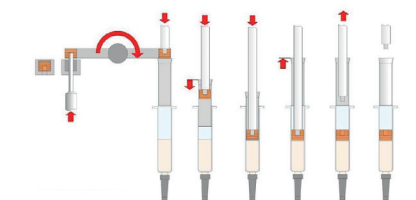
Conclusion

The seal integrity of all new plunger designs was good and their He-leak rate far below the Kirsch criterion. The outer diameter of the redesign plungers was identical to the initial one (Ø = 20.0mm)

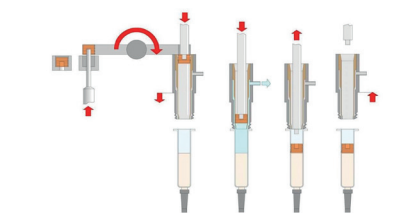
The selected new design (V9547) showed very positive effect concerning the BLF (always below 15N after 1 month at 40°C). Also the gliding force of the new design was consistently <2N.

Standard Process

Stopper insertion via vent tube and rod



Stopper insertion via vacuum



Schemes courtesy of Syntegon

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