Evolving Component Technologies to Meet the Needs of Large Volume Injections

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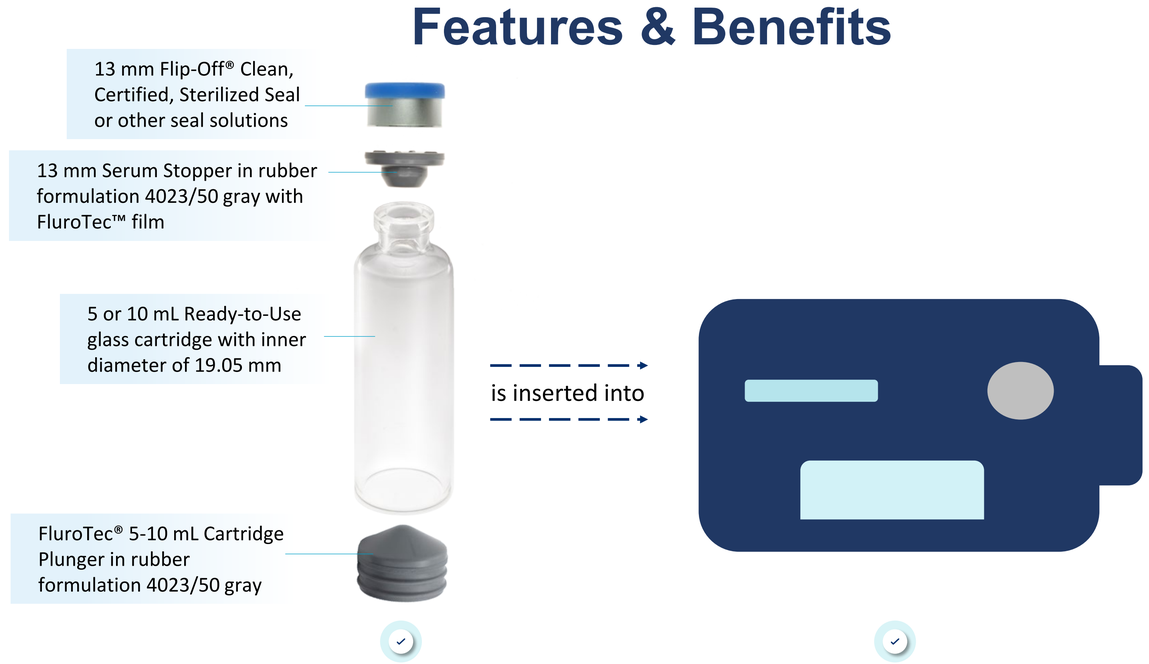
Introduction

As the pharmaceutical industry continues to see significant growth of drug products developed in cartridges, there is a trend for pharmaceutical companies to evaluate more complex drug molecules that require higher injection volume or viscosity. These complex biological molecules are typically intended for self-administration by the patient and integrate a prefilled syringe or a prefilled cartridge with a delivery device to optimize safety, dose accuracy, and ease of use. Innovations in the device space for large volume On-Body Delivery Systems (OBDS), such as bolus injectors, have allowed for delivery of protein-based therapies up to 10 mL and higher. One challenge, however, is that existing plunger and seal technology for cartridges was developed for less complex drug molecules and does not meet the evolving requirements for drug delivery, especially for drug compatibility and injection force. In response to the market needs for plunger technology designed especially for large volume injectors, West has developed a 5-10 mL FluroTec® film laminated cartridge plunger (West Article 2360).

Features & Benefits



Assembled, filled large volume (5 or 10 mL) glass cartridge

An OBDS for self-administration which can move treatment from hospital to home

- ✓ Drug contact with SAME FluroTec™ film & elastomer for plunger and stopper to simplify development:
  - ❖ Minimizes extractables and leachables
  - ❖ FluroTec™ film and rubber formulation extensively proven in the market
- ✓ Tested glass cartridge components showed excellent performance
- ✓ The FluroTec® 5-10 mL Cartridge Plunger mitigates potential risk to patients and enables a smoother journey to market of large volume on-body delivery systems

FluroTec® 5-10 mL Cartridge Plunger Performance Testing

Test speed: 50 mm/min described in ISO 11608-3:2012

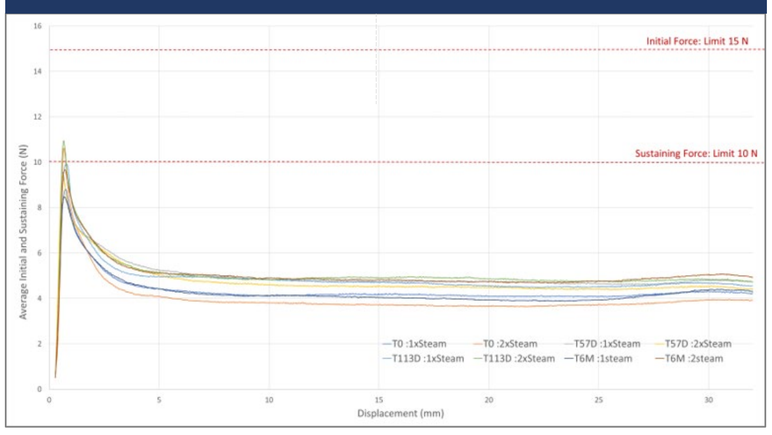


Figure 1: *50mm/min at multiple time points; 1x and 2x steam sterilization treatment, each curve is the average of 10 tested cartridges from Glass Vendor 1. The Initial Force is taken up to 2 mm and the Sustaining Force is taken from 2 mm to 30 mm. Liquid was removed prior testing*

Test speed: 3.5 mm/min

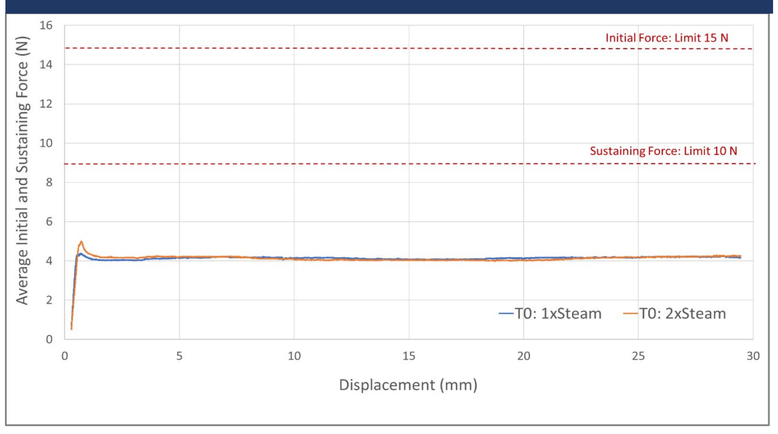


Figure 2: *3.5 mm/min conducted at T0 only, with 1x and 2x steam sterilization treatment; each curve is the average of 10 tested cartridges. The Initial Force is taken up 2 mm and the Sustaining Force is taken from 2 mm to 30 mm - test speed representative of real use case: large volume injection time ~ 15 – 20 min. Liquid was removed prior testing.*

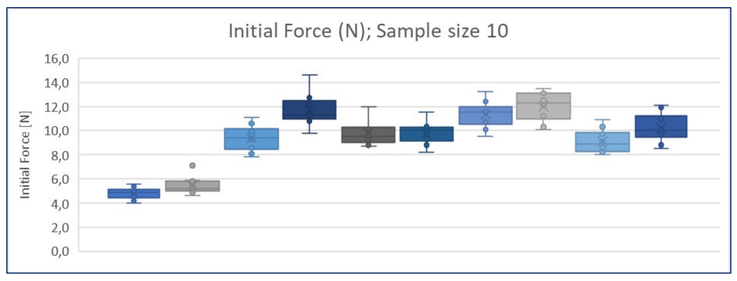


Figure 3: *Comparison of Average Initial Force: all time points, all speeds [1x means 1 time and 2x means two times steam sterilization].*

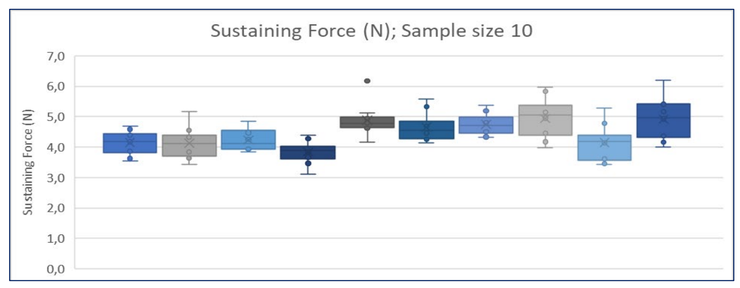


Figure 4: *Comparison of Average Sustaining Force: all time points, all speeds [1x means 1 time and 2x means two times steam sterilization].*

Results:

- Forces are consistent and far below requested limits over time for 1x and 2x steam sterilized plungers, all speeds 50 and 3.5mm/min.
- The initial force increases by 4 - 6 N as the speed of the test increased from 3.5 mm/min to 50 mm/min, at the same time an impact on sustaining force is negligible.
- The impact of double steam sterilization cycle, representing a worst-case scenario, on higher initial forces could be demonstrated with an increase of 1-2 N compared to 1x steam sterilization.

Disclaimer: Data is provided for informational purposes only. It is the customer's responsibility to evaluate and test the product to determine its compatibility with other materials and fitness for any end use.

Container Closure Integrity [CCI]

He Leak rates measurement of Art. 2360 in 10 mL glass cartridges

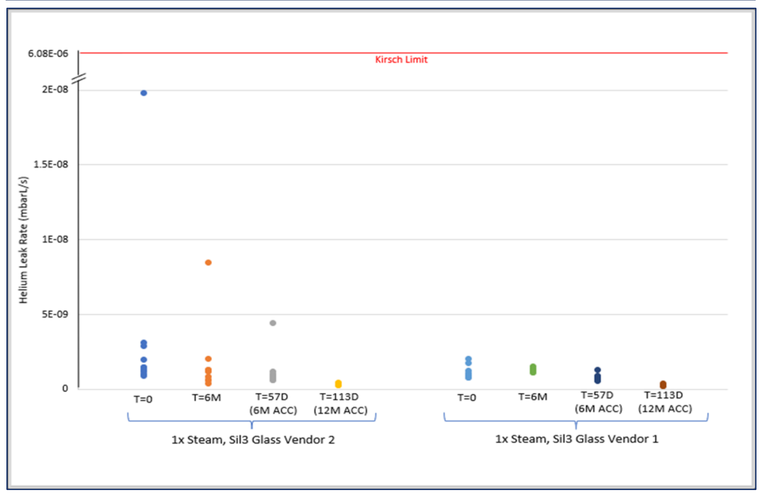


Figure 5: *Container Closure Integrity Test, Helium Leak rates measurement of Article 2360 in a 10 mL glass cartridge.*

Results:

- All Helium leak rates of the container closure systems (CCSs) were **far below the Kirsch limit** for all test points and for both glass cartridges from vendor 1 and vendor 2.
- The results are about 1000 times lower than the Kirsch limit.

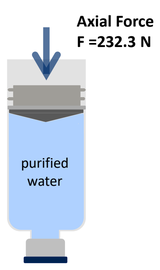
Fluid Leakage

Sample Timepoints	Number of failed samples / total number of tested samples – 1x steam sterilized	
	Glass Vendor 1	Glass Vendor 2
T0	0/10	0/10
T1 acc [57 days]	0/10	0/10
T2 acc [113 days]	0/10	0/10
T6 months	0/10	0/10
T12 months	results outstanding	results outstanding
T24 months	results outstanding	results outstanding

Figure 6: *Plungers stored in bulk [bag] under controlled ambient RT [23±3°C] monitored humidity or accelerated 40°C/75% RH stability storage conditions.*

Results:

- No fluid leakage observed over time



Pre-Machinability Testing with Selected Format Parts

- ❖ Trials at the external machine vendor used standard sorting systems with a test bunker and sorting bowl for a 1-3 mL siliconized syringe plunger.
- ❖ West used existing format parts not specially designed for Article 2360 including a vibratory sorting bowl.

Figure 7: *Plungers moving well orientated up the Vibratory Sorting Bowl - the image is property of Syntegon*

Observations:

External machine vendor:

- Successful radial movement around bowl & track up feed rails
- Successfully buffered on a distributor plate
- Enough back pressure in the outlet to reach speed
- Expected to be transportable on linear conveyer belt
- Plungers can be sorted with standard sorter system used typically by the machine vendor.

Internal at West:

- Successful radial movement around bowl & track up feed rails
- Able to be tracked on crown and on cavity side
- Minimal back pressure required to move plungers
- No observation of twinning
- No visible particulates were observed during or after study