Break Loose Force and Glide Force Evaluation of Various Container Closure System Combinations

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Abstract/Introduction

A comprehensive evaluation of break loose force and glide force (BLGF) was conducted on 1 ml long (L) and 2.25 ml empty prefillable syringes (PFS, for biologics) from three vendors in combination with four to five types of plunger stoppers from four vendors. Fifteen container closure system (CCS) combinations were assessed for both the 1 mL L syringes and for the 2.25 mL syringe, respectively. Potential factors that might impact BLGF were investigated, including key dimensional analysis of the syringes and plunger stoppers and the measurement of silicone oil content and distribution within the syringes. However, the properties of the plunger stoppers, such as the plunger stopper design, formulation, and manufacturing process, may impact the BLGF performance. The results indicate that variation in silicone oil levels does not affect CCS BLGF performance. The comparisons of different CCS combinations provide valuable insights into the basic BLGF performance of syringes and plunger stoppers from different vendors.

Methods

BLGF Test

The drug product development (DPD) department laboratory at WuXi Biologics executed and reported the BLGF test. A material testing machine (Instron:2344) with fitting accessories was applied to perform the BLGF test. The following table lists the basic test parameters.

Load cell	100 N
Crosshead speed	200 mm/min
Data acquisition frequency	65 Hz
Preload	0.2 N
Preload cross head velocity	20 mm/min
End of test criteria	30 N

Stoppers were preset in empty syringes at least 12 hours before testing. The depth of the stoppers was determined based on the stopper position for 1 mL water in a 1 mL L syringe and 1.7m L water in a 2.25 mL syringe. Additionally, the plunger stopper insertion depth (PSID) was set at approximately 11–12 mm for 1 mL L syringes and 12–13 mm for 2.25 mL syringes. Plunger rods were inserted at least 30 minutes before testing. Samples were placed under testing conditions (23℃ ± 5℃ temperature and 50% ± 25% humidity) for at least 30 minutes before testing.

Silicone Oil Measurement

The evaluation of silicone oil content and distribution in 1 mL L and 2.25 mL syringes was conducted using Bouncer (Unchained). The test was performed in binary (BI) mode. The instrument captured measurements at 30-degree intervals, collecting data across up to 12 lines in total.

Key Dimension Measurement

Inner diameter of syringe and maximum diameter of plunger stopper were measured with an image dimension measurement system.

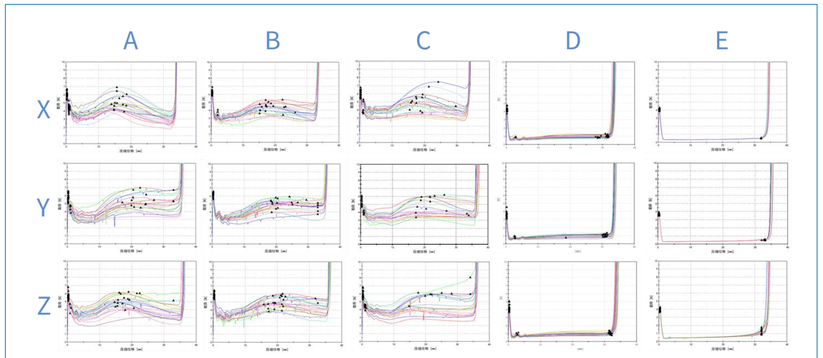
Results

BLGF Test Results of 1 mL L PFS CCS

No.	Syringe
1	X
2	Y
3	Z

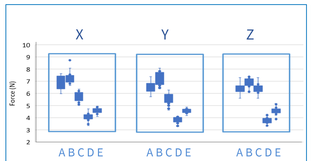
No.	Plunger Stopper
1	A*
2	B*
3	C*
4	D
5	E

*A, B, and C share the same plunger stopper design drawing, formulation, and coating.

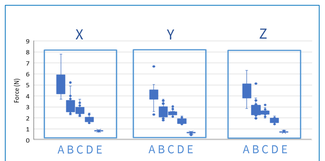


BLGF diagram of a 1 mL L CCS combination for an empty PFS

- For each type of plunger stopper, BLGF performance is consistent among the three syringes.
- For the plunger stoppers sharing same design, formulation and coating, BLGF performance of plunger stopper B was slightly better than the other two plunger stopper (A & C)in each syringe group with lower variation. The differences among the three stoppers are the washing process , siliconization process, sterilization method and package.
- Plunger stopper E showed best BLGF performance, with plunger stopper D coming in second.



Break loose force of a 1 mL L CCS



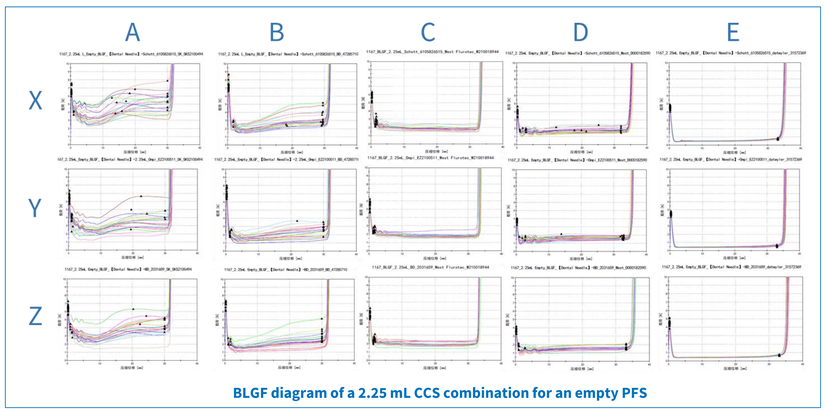
Max glide force of a 1 mL L CCS

BLGF Test Results for 2.25 mL PFS CCS

No.	Syringe
1	X
2	Y
3	Z

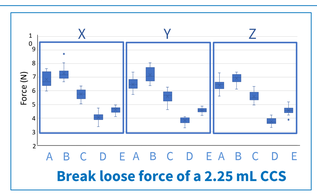
No.	Plunger Stopper
1	A*
2	B*
3	C*
4	D
5	E

*A, B, C share the same plunger stopper design drawing, formulation and coating.

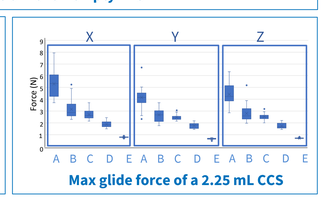


BLGF diagram of a 2.25 mL CCS combination for an empty PFS

- For each type of plunger stopper, BLGF performance is consistent among the three syringes
- For the plunger stoppers with same design, formulation and coating, BLGF performance of plunger stopper C was the best, while the one of A was the worst. The differences among the three stoppers are the washing process , siliconization process, sterilization method and package.
- Plunger stopper E showed the best BLGF performance, with plunger stopper D achieving second.



Break loose force of a 2.25 mL CCS



Max glide force of a 2.25 mL CCS

Silicone Oil Measurement

Silicone oil distribution and content of a 1 mL L syringe

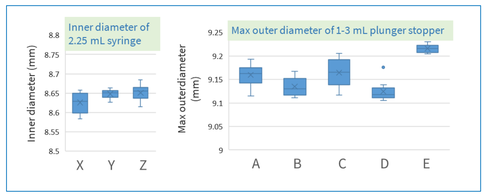
Syringe	Time since manufacture	Silicone Oil Distribution Graph	Silicone Oil Content
X	24M		218±7 μg
Y	28M		216 ±9 μg
Z	39M		173 ±9 μg

Silicone oil distribution and content of a 2.25 ml syringe

Syringe	Time since manufacture	Silicone Oil Distribution Graph	Silicone Oil Content
X	29M		271±10 μg
Y	15M		333±22 μg
Z	12M		461±20 μg

- Silicone oil content of the 1 ml L syringe Z and 2.25 mL syringe X was the lowest in each group, which mmighty be attributed to the longer time elapsed since manufacture.
- Although the silicone oil content varied between syringes, the difference had little impact on BLGF performance among the three syringes with the same plunger stopper.

Key Dimension Measurement



- The three syringes had a similar inner diameter, and the difference was within 0.1 mm.
- Plunger stopper E had the largest maximum outer diameter, but the difference among the plunger stoppers was also within 0.1 mm.

Conclusion

- For the same plunger stopper, the syringes from the three vendors showed little impact on BLGF performance. In addition, the variation of silicone oil content in the syringes did not affect the BLGF performance either.
- For each syringe group, the BLGF performance varied obviously among the plunger stoppers. The differences in design, formulation, and manufacturing processes of the plunger stoppers may play a dominant role in BLGF performance.

References

N/A

About WuXi Biologics

WuXi Biologics is a global leading contract research, development, and manufacturing organization (CRDMO) offering end-to-end solutions to enable partners to discover, develop and manufacture biologics from concept to commercialization.

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