Innovative Dual Chamber Blow-Fill-Seal (BFS) Injection System Development:

A Collaborative Case Study by ApiJect and PSN Labs

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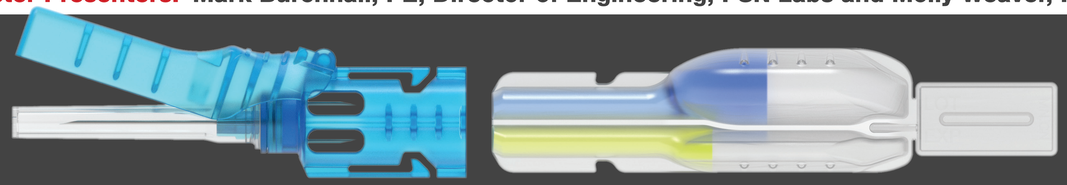


Introduction

ApiJect is developing a dual chamber Blow-Fill-Seal (BFS) device to aseptically deliver tw o different drugs in a single injection. BFS Needle Injection systems have advantages over other pre-filled drug delivery devices as they are inherently more scalable, sustainable, and cost-effective.

ApiJect has partnered with PSN Labs to assist in the development of this dual chamber device. PSN Labs primarily supports clients in the medical device and pharmaceutical industries and is an ISO 9001:2015, ISO 17025:2017, and ISO 13485:2016 certified facility.

The goal of the dual chamber device development is to leverage computational modeling and simulation (CM&S), rapid prototyping, benchtop testing, and usability studies to rapidly develop a device that delivers drugs to patients in a scalable, low-cost design.

Typical requirements derived from ISO 11608-1:2022 and ISO 11608-3:2022 and include:

- Delivery time of less than 10 seconds
- Ensure delivery of 2.7 mL of the total drug product (2.0 mL and 0.7 mL)
- Meet ergonomic requirements for the user
- High reliability targets in variable environments

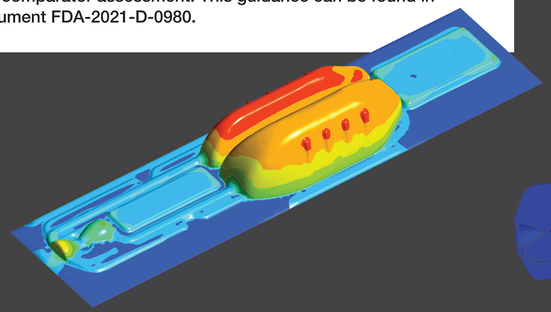
*The ApiJect Dual Chamber BFS Device and its components are not cleared by the FDA or other regulatory bodies.

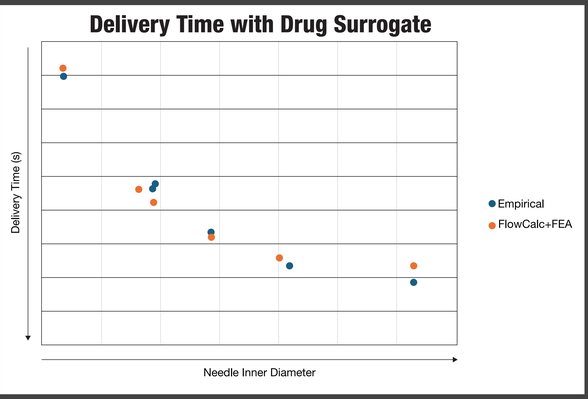
Methods

PSN Labs evaluated the constitutive properties of the low-density polyethylene (LDPE) BFS package and the polypropylene needle hub to ensure that the mechanical properties of the package could be assessed at various conditions, including shelf-life, delivery environmental conditions, sterilization, and rate-dependent interactions.

CM&S was utilized to evaluate multiple device properties, but the focus of this poster is the delivery time and squeeze force of the BFS vial needle injection system. Computational Fluid Dynamics (CFD) models were developed to simulate the thickness of the LDPE BFS container. Finite Element Analysis (FEA) was performed on the mapped thickness properties to assess the squeeze force and determine pressures in the drug delivery model. Drug delivery performance was evaluated by inputting these pressures into a parameterized closed-form analytical model that output the time of delivery. The output of this model was compared to physical test data obtained through rapid prototyping.

PSN Labs and ApiJect followed FDA guidance on leveraging CM&S for regulatory evidence generation during analysis and comparator assessment. This guidance can be found in document FDA-2021-D-0980.

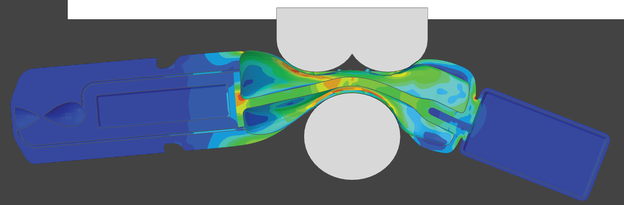




Results

A system-level model was utilized to optimize the delivery profile of the dual chamber BFS. The results indicate that the model was within 8% of the prototype data on average for delivery time when a drug surrogate was used. The model predicts that drug delivery will occur within 7.0 s at a force of 38.4 N under nominal dimensional and environmental conditions. In environmental extremes (from 2°C to 40°C), with drug viscosity ranging from 0.75 to 3.76 cp and dimensional variations, the delivery time may shift to 5.5 – 7.8 s, as predicted by the model.

These values are considered to meet the specifications outlined for the development of this device. The model was also leveraged to ensure that the drug delivery profile of the device would equally empty various volumes of the drug product.



Discussion & Conclusion

While the use of Computational Modeling and Simulation (CM&S) to evaluate multiphysics functions in medical and drug delivery device development is not novel, applying these models to assess standard testing requirements for needle-based injection systems enables the rapid development of alternative delivery systems, such as the ApiJect BFS Needle Injection System. By directly correlating design inputs to CM&S, novel injection systems can be developed more quickly, reducing prototyping costs and ensuring higher functionality in these designs.

For BFS vial development, drug packaging can take time and cost to produce a first-molded prototype (although still considerably less than a novel syringe). Therefore, it is crucial to ensure that each prototype iteration is as robust as possible.

Future Directions

Although still in development, the models created to evaluate essential drug delivery outputs and basic safety requirements were designed to be leveraged for regulatory evidence generation. By utilizing these models to replace some design verification testing, drug delivery device manufacturers can reduce prototyping needs, minimize testing time, and provide evidence for conditions that are difficult to test.

These methods lead to the development of devices that are more effective and safer for patients as they enter the market.