apiject™

INTRODUCING THE APIJECT™ PREFILLED INJECTOR

A Prefilled Blow-Fill-Seal Parenteral that Delivers a 0.1mL – 2.0mL Dose

THE APIJECT PREFILLED INJECTOR

A 2-part system, made up of a Blow-Fill-Seal (BFS) Container prefilled with the drug dose, and a Needle Hub with a Connector pre-attached.

1 Needle Hub

2 Blow-Fill-Seal (BFS) Container

Overview

The ApiJect Prefilled Injector is a combination parenteral system that can administer a 0.1mL to 2.0mL delivered dose on a 0.2mL to 2.1mL fill.

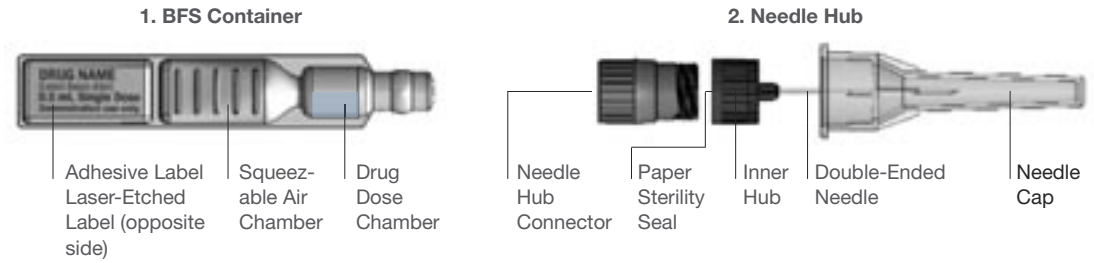
The parenteral is a two-part system, made up of a Blow-Fill-Seal (BFS) container prefilled with the drug dose, and a Needle Hub with a Connector pre-attached. When these components are snapped together and activated using a simple twist motion, the user is able to squeeze the drug out of the BFS container and through the needle.

This document will describe in reasonable detail the ApiJect Prefilled Injector and the general manufacturing process used to produce it. If further information is needed, please see the final page for contact information.

Please note: ApiJect is also developing a three-part Prefilled Injector for which the Needle Hub and Needle Hub Connector are shipped separately. This three-part device is being developed for an emergency COVID-19 response effort in coordination with the U.S. Department of Defense and the U.S. Department of Health and Human Services. All of the information in this booklet will be specific to the two-part Prefilled Injector unless otherwise noted.

Device Breakdown

The ApiJect Prefilled Injector is made up of two primary components, each of which has several sub-components.

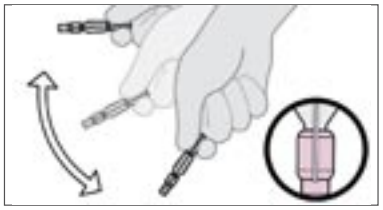


The BFS Container for the ApiJect Prefilled Injector is made of pharmaceutical-grade low-density polyethylene (LDPE). The needle is made of stainless steel. The label is made of paper and uses an adhesive that is common with BFS. And the remaining components, excluding the drug dose, are made of polypropylene.

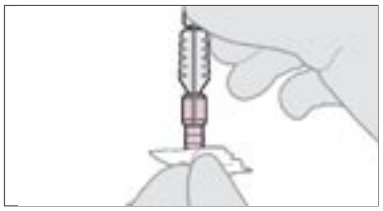
Intended Use

The ApiJect Prefilled Injector is assembled, delivers a single dose, and is then discarded into a sharps disposal container. The following diagram walks through its intended use.

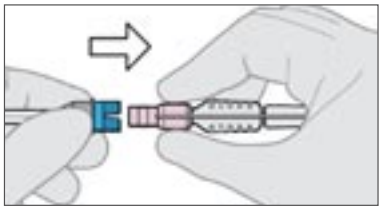
Please note: This is for demonstration purposes only and is not meant to represent an approved IFU. The three-part ApiJect Prefilled Injector will require additional steps.



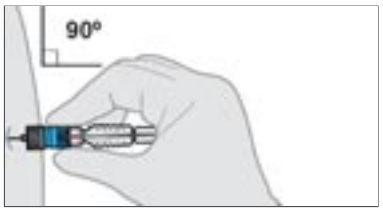
1. ***Whip the Drug Forward***
   Whip the BFS Container downwards so all of the drug product is in the small front chamber (i.e., the chamber nearest the Needle Hub and Connector attachment point).



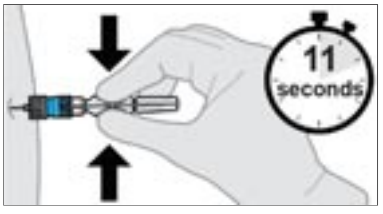
2. ***Clean the Container***
   Clean the Container's tip with an alcohol wipe.



3. ***Attach Needle Hub and Activate***
   Firmly push the Needle Hub with the pre-attached Connector to the BFS Container until you feel a "click." Then, holding the Connector, twist the Needle Hub clockwise until it stops. Device is now activated.



4. ***Remove the Cap and Insert***
   Remove the Needle Cap. Grip the device near the Connector and insert into the deltoid muscle.



5. ***Squeeze and Hold to Inject***
   Firmly squeeze the large air chamber on the Container. Hold the squeeze for 11 seconds to inject all of the liquid. Once complete, properly discard the Prefilled Injector.

The BFS Container

The primary packaging used for the ApiJect Prefilled Injector is a Blow-Fill-Seal (BFS) Container that is reliably and aseptically filled with a single of the injectable drug.

About Blow-Fill-Seal

In 2004, the FDA issued guidance that BFS is an advanced aseptic process for packaging drugs[1].

A 50+ year-old technology, BFS has found a home in drug packaging. Every year, BFS packages more than 50 billion doses of biologics, oral vaccines, pharmaceuticals and other sterile liquids. Notable examples of drug products that have been successfully tested in BFS, many of which are on the market, include rotavirus, RSV, and influenza vaccines, as well as biologics such as Albuterol, Tiotropium, Dornase alfa, and Budesonide.

While each BFS machine uses the same general process, the following manufacturing description uses a Rommelag® bp460-15 BFS machine as its model.

In a 3-second automated process, the BFS machine vacuum pulls on a sheet of molten polymer resin, low-density polyethylene (LDPE) being expelled from a parison to create a strip of 12-25 primary containers, aseptically fills those primary containers with the drug product, and then seals them – all within an ISO class 5 environment. Depending on the drug product, the air chamber contains either sterile air or Nitrogen. The temperature of the drug is carefully monitored and controlled throughout the process. Up to 15 million doses a month can be packaged with a single machine. In addition, BFS allows for rapid scaling of production, and a full changeover from one drug product to another, including flushing, cleaning, and mold change, can typically be done in as little as 6-72 hours.

Blow-Fill-Seal (BFS) Container

The BFS Container in the ApiJect Prefilled Injector can be aseptically filled with a delivered dose of 0.1mL – 2.0mL. The mold to create the BFS container is designed with two connected chambers: a smaller top chamber where a dose of the drug product is filled, and a larger bottom chamber that houses the sterile air to drive the injection.

The top chamber is designed so that once the liquid is flicked by the nurse into the top chamber, it will have a very difficult time falling back into the larger bottom chamber. The chambers and the labeling area vary in size based on the delivered dose. ApiJect currently uses three different molds based on the dose size: 0.2-0.65mL fill, 0.7-1.2mL fill, and a 1.2-2.1mL fill.

BFS Container

Heat Sensitivity

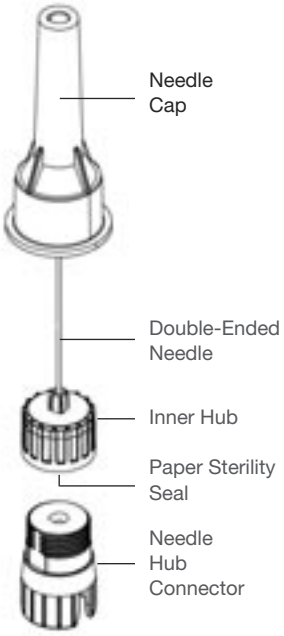
As part of the BFS process, just moments after the BFS Container is formed into its shape, drug product is injected into the cooling plastic container. As a result, some have historically seen BFS as a risky process for temperature-sensitive drug products. However, BFS has always been able to handle a wide range of drug products, including most biologics, and further advances in BFS and mold design technology have made temperature management even better.

[1] https://www.fda.gov/media/71026/download

Factors that can be adjusted in order to best control the temperature change of the drug product include the wall thickness and design of the BFS Container, mold shape, the use of jacketed drug formulation tanks and built-in features of the BFS machine that facilitate even faster rapid cooling of the drug product immediately upon entry into the BFS Container.

The Needle Hub

The Needle Hub for the ApiJect Prefilled Injector is based on a pen needle design, adapted for the soft-plastic characteristics of the LDPE-based BFS Container.



Components

The Needle Hub is made up of five principle components, which are all assembled by machine during the manufacturing process:

- Triple-bevel, double-ended hypodermic needle (stainless steel)
- Inner Hub (polypropylene)
- Needle Cap (polypropylene)
- Paper Sterility Seal (paper)
- Needle Hub Connector (polypropylene)

Needle Characteristics

The ApiJect Prefilled Injector uses a triple-bevel, double-ended needle, manufactured by Tae-Chang Industrial® of South Korea. The triple bevel both reduces patient pain from the needle insertion and allows for a cleaner activation of the injector.

The Needle Hub can be affixed with the following range of hypodermic needles, based on the patient and drug delivery requirements:

- Pediatric IM: 5/8” (16cm) 23 G needle
- Adult IM: 1” (25mm) 23 G needle
- Large Adult IM: 1½” (28mm) 23 G needle

The Double-Ended Needle pierces the BFS Container

Activation

Once the Needle Hub has been pushed onto the BFS Container (see Intended Use section), the nurse or healthcare professional will twist the Needle Cap to activate the Prefilled Injector.

Activation occurs because the twist motion drives the bottom end of the double-ended needle through the paper seal that keeps the needle sterile, and into the top of the BFS Container. The needle only goes slightly into the container in order to minimize wastage.

Three-Part Prefilled Injector

In the three-part ApiJect Prefilled Injector, the Needle Hub and the Needle Hub Connector arrive separately. The healthcare professional will push the Needle Hub Connector onto the BFS Container first, and then screw on the Needle Hub.

Future Versions

ApiJect is working on future variations on the Prefilled Injector. These include Prefilled Injectors for doses larger than 2.1 mL fill, alternate ergonomic Container shapes, and a Prefilled Injector where the Needle Hub with Connector come pre-attached to the BFS Container for an even simpler activation process.

The Manufacturing Process

One of the many strengths of the ApiJect Prefilled Injector is the versatility and efficiency of its manufacturing process. Blow-Fill-Seal allows for the entire fill and finish packaging of the drug to take place in a single machine, while the Needle Hub and Connector are made in an ApiJect facility and shipped to the final destination.

Alternative Supply Chain

The ApiJect Prefilled Injector is manufactured using a different, much simpler supply chain than traditional glass vial or prefilled syringes. Made from only two raw materials – pharmaceutical-grade plastic resin and steel for the hypodermic needles – the entire supply chain can often be locally sourced.

In addition, its compact and domestic nature allows for this alternative supply chain to be much more robust, and the two raw components can be stored in large quantities at manufacturing facilities.

Fill & Finish

The two primary components of the ApiJect Prefilled Injector, the BFS Container and the Needle Hub, are manufactured independently.

The manufacturing space for the BFS Container is relatively small, typically around 5,000 sq. ft. of GMP space. While the manufacturing lines and exact process will vary by location, it follows this general process:

1. ***BFS Machine*** – First, the prepared bulk drug is filled and sealed into a BFS container by a BFS machine. At this time, ApiJect uses Rommelag® bp460-15 and bp434 BFS rotary machines which produce strips of 25 Containers, but this amount can vary based on container shape and pharmaceutical company needs.

2. ***Laser-Applied Label*** – As each strip of containers emerge from the BFS machine and enter the "punch machine" (see step #3), the lot number and expiration date are laser-etched onto one side of the label tab of each BFS Container.

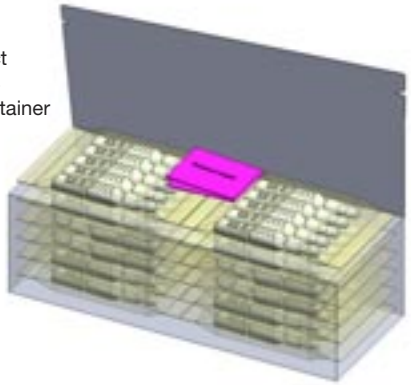
3. ***Punching and Separation*** – Once the laser-etched strip of BFS containers is released from the BFS machine, the excess plastic trim is "punched" away, and then the strip of 25 BFS containers is separated into 5-container "cards." The containers will remain as 5-unit cards unless the pharmaceutical company has special needs.

4. ***Leak Detection*** – After separation, each card is taken through a leak detection process using a vacuum decay method to check for any leaks to the BFS Container. All of these steps are built in-line with the BFS machine and do not slow down the manufacturing output.

5. ***Visual Inspection*** – Next, each card is taken through both automated and manual visual inspection processes to detect particulates. Please note, unlike glass, BFS generates few to no particulates. Plastic does not delaminate and no vial stopper is required so the materials cannot be a source of the particulates.

6. ***Adhesive Drug Label*** – If required, an adhesive label may also be applied to the label tab, opposite of the laser-etched side per step #2, on each BFS Container.

7. ***Pouching*** – Finally each card is pouched within foil wrap. This overwrap helps avoid vapor loss and protects against sunlight exposure. The labeling instructions are preprinted on the foil.


60 ct BFS Container Box

Packaging

ApiJect has designed its BFS Containers for efficient cold-chain storage. Each card of five containers is designed to stack on top of one another, even in the foil pouch.

In general, ApiJect expects to load 12 cards to a carton, 12 cartons to a case, and 64 cases to a U.S. pallet – bringing the total number of doses per pallet to 46,080. The carton, which will be serialized for tracking, will also contain any IFU and other instructional material, as required. While packaging configurations may vary by project, ApiJect currently estimates each BFS container (1 dose) will take up 7-20 cm^3 of space in the cold chain.

Location of Production

The BFS Container can be manufactured in a variety of places. ApiJect provides both setup and mold-design support for all of these options:

- ***ApiJect's Factories*** – ApiJect is in the process of building its first facility. Located in North Carolina, it is scheduled to come online starting in Q1 2022. It will be able to handle GMP and BSL-2 drug products, with both cold-chain and freeze-chain capabilities, potent compounds and DEA controlled substances, and can serve any size job.

- ***Pharmaceutical Company's Facilities*** – If the pharmaceutical company prefers, they can build a complete BFS manufacturing line in their own facilities by licensing ApiJect process knowledge, thus giving them full oversight of the drug filling process.

- ***Trusted 3rd Party Drug Manufacturer*** – Third party CMOs and CDMOs can also install BFS manufacturing lines in their facilities, allowing them to better serve current clients while also attracting new customers.

The Needle Hub and future additional components that ApiJect will manufacture in the coming years are produced solely by ApiJect to ensure quality. The correct size and order volume of Needle Hubs will be produced by ApiJect and shipped to the final location specified by the pharmaceutical partner.

Regulatory Pathways

At this time, neither the FDA nor any other regulatory agency has cleared our Prefilled Injector or the Needle Hub for distribution in the United States or any other market. The following explains our path forward.

510(k) Filing

ApiJect is in the process of filing for a 510(k) with the U.S. FDA on the Needle Hub with the Connector. This initial filing is for the three-part ApiJect Prefilled Syringe, as per our work with the U.S. Government on COVID-19 response.

Pharmaceutical Company Testing

The pharmaceutical company that owns the drug would still need to take their drug in the BFS primary packaging through FDA or other relevant-market regulatory clearance. As part of that process, the drug would need to be filled in the chosen BFS Container and put up on stability testing. If requested, ApiJect would work with the pharmaceutical company on this process, providing guidance and mold selection and customization services.

Human Factors

At this time, ApiJect is taking its three-part Prefilled Injector through human factors testing. The process is showing positive results, but it is not yet complete. Human factors testing for the two-part Prefilled Injector will begin sometime in Q4 2020.

Future Development

ApiJect continues to invest significant resources in research and development. These efforts are primarily focused on various mold configurations for the single-dose ApiJect Prefilled Injector, other types of BFS-based Injectors, and add-on components to enhance the capabilities of our Injectors.

In the coming months and years, ApiJect looks forward to rolling out these additional products and components that will help our pharmaceutical partners expand their drugs into more markets so more people in the world can receive the medicines and vaccines they need.

Introducing ApiJect

ApiJect Systems, Corp. is a medical technology company that is transforming how people get medicines and vaccines. By using well-established technologies in surprising new ways, ApiJect's Technology Platform makes it fast and easy for pharmaceutical companies to package their drugs in interlocking injection systems that can be quickly manufactured at enormous scale.

Our first product, the ApiJect Prefilled Injector, is a single-dose prefilled injection device that is created when a healthcare worker screws a Needle Hub onto the top of a Blow-Fill-Seal (BFS) Container, aseptically prefilled with a medicine or vaccine. Simple, scalable devices like the Prefilled Injector will enable ApiJect to carry out its mission of making injectable medicines safe and available for everyone.

More Information

For more information on the ApiJect Prefilled Injector or ApiJect's manufacturing services, please contact Ray Sell, VP of Business Development, at rsell@apiject.com.