apiject™

Introducing ApiJect:

The world's first BFS-enabled, prefilled "soft syringe"

A brief overview of an innovation for injection technology that can save lives and stretch healthcare budgets farther.

Standard syringes and 10-dose glass vials won't get us where we need to go.

Syringes and multi-dose vials have helped create enormous progress in public health. But today they are part of the problem.

The world health community has made astounding progress toward universal coverage for medicines and vaccines over the past 100 years. Of the tens of billions of medical injections given each year, about 5% are vaccines.[1] According to Gavi, 70% of the world's children are now immunized with all recommended vaccines.[2] It's one of the great accomplishments of the past century... and the global health community is working hard to finish the job.

But the standard syringe and multi-dose vial – two essential tools in achieving today's public health success – are now part of the problem. All too commonly syringes are re-used, contaminating not only the used syringes, but also the contents of the multi-dose glass vials that fill those and other syringes.[3] As a result, more than 3 million people are killed each year and another 20+ million are infected with life-altering diseases.[4]

The global health community recognizes the safety issues that come from multi-dose vials and syringes. They have tried to use more single-dose formats, most notably Uniject™, the world's first compact Prefilled Auto-Disable syringe (cPAD).[5] But multi-dose vials are by far the least expensive option and remain the most popular.

In order to both eliminate unsafe injections and cover every child, the global health community needs a single-dose injection format that costs less per dose delivered than a multi-dose vial plus syringe.

The Problem of Multi-Dose Vials in Two Charts:

1. Contaminated multi-dose vials or syringes in clinical settings infect millions yearly.

When a health worker inserts a contaminated needle into a multi-dose vial to withdraw a vaccine or medicine, the needle contaminates all remaining doses in that vial. After that, every injection from that vial – even using clean needles or auto-disabling syringes – infects patients.

Table 1 [6]

Disease or infection	Est. % of new cases caused by unsafe injections	Est. # of patients infected per year
Bacterial	7%	3 million
Hepatitis B	25%	15 million
Hepatitis C	8%	1 million
HIV	14%	340,000+
Top 20 diseases/infections	5-10% est.	10's of millions

2. Children are turned away from vaccine clinics when health workers don't want to open new 10-dose vials because they fear wastage. Two case studies:

Health workers in many low-income countries wait until "enough" children are present to justify opening a vial. Often many children are turned away. Some patients never return, as shown in these studies from just two countries based on representative samples of health facilities.[7]

Table 2 [8]

	Cambodia	Nigeria
Average vaccine wastage rate in health centers (measles example)	58%	19%
Average number of children who must be present before health workers agree to open a vial	2.2	6.2
Proportion of parents saying they were turned away for vaccination	4%	30%
Proportion of those turned away who never received vaccine	12%	53%
Vaccines missed among those turned away	MCV: 63%	BCG: 33% MCV: 26%

ApiJect is a New One-Dose Format Designed to be the Lowest-Cost and Safest Option.

By using Blow-Fill-Seal (BFS) technology to create a prefilled syringe, ApiJect can help the world achieve 100% coverage economically and eliminate unsafe medical injections.

A new type of single-use prefilled syringe is about to become available in the second half of 2020. Called ApiJect, it is a simple yet sophisticated mono-dose system that costs less per dose upfront and also costs up to 50% less per dose delivered depending on wastage costs.[9]

The ApiJect prefilled syringe combines (1) a medical-grade plastic container that is made and filled using "Blow-Fill-Seal" (BFS) with (2) a plastic Needle Hub.[10] The result is an ultra-low-cost prefilled syringe that cannot spread disease, is hard to counterfeit, and simple to use.

BFS plastic manufacturing technology has been widely used for more than 50 years. BFS is a high-efficiency, low-heat, low-cost, aseptic manufacturing method used to produce a wide range of liquid-filled containers.

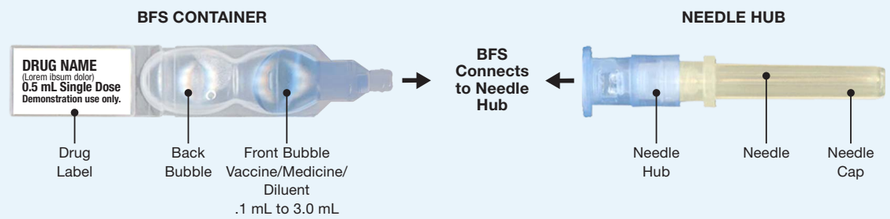
BFS has been growing in regulatory acceptance over the last 20 years. Billions of eyedrop and eardrop bottles are aseptically produced every year using BFS, and several respiratory and oral medications are packaged in it, including a rotavirus vaccine.

Marc Koska, the inventor of the K1 safe syringe and the founder of ApiJect, invented a way to add a needle to a BFS container, transforming it into a prefilled syringe.

Mr. Koska recognized that BFS was much more affordable than the multi-step "Form-Fill-Seal" process used for Uniject™ and had numerous cost and safety benefits over manufacturing of glass vials and traditional barrel-and-plunger type syringes.

With the ApiJect syringe, now health ministries and healthcare providers can have the lowest-cost injection format without sacrificing safety.

APIJECT™ BFS PREFILLED SYRINGE



Comparing the Total Cost per Dose of Vaccine Delivery[11]

Costs shown do not include cost of vaccine injected

ApiJect can achieve large savings that will allow it to be priced at or below a 10-dose glass vial thanks primarily to the efficiency of BFS manufacturing, less overfill, much faster injection prep, and its light, compact size.

Note: Drug price of 25¢ per dose used to calculate overfill, breakage, and waste.

	Purchase Cost (Upfront)	ApiJect	10-Dose Vial per dose	Uniject™	1-Dose Vial
1	Manufacturing	$0.05	$0.155	$0.55	$0.45
2	Overfill + Sterilization	$0.02	$0.07	$0.06	$0.15
3	VVM* (if required)	$0.05	$0.05	$0.05	$0.05
4	**UNICEF** vaccine purchase price	**$0.12** *diff. +/-*	**$0.23** *+91%*	**$0.66** *+464%*	**$0.65** *+453%*
6	Syringe/Needle Hub (ex. shipping)	$0.20	$0.04	$0.00	$0.04
7	Safety Box + Shipping	$0.05	$0.10	$0.05	$0.32
8	**Purchase Cost per Dose**	**$0.37** *diff. +/-*	**$0.37** *0%*	**$0.71** *+94%*	**$1.01** *+175%*
	Field Costs (In Country)				
9	Cold Chain + Transit Costs	$0.34	$0.30	$0.71	$0.59
10	Labor, Breakage & Disposal	$0.11	$0.23	$0.11	$0.27
11	**Field Cost per Dose**	**$0.45** *diff. +/-*	**$0.53** *+18%*	**$0.82** *+82%*	**$0.86** *+91%*
12	**Total Cost/Dose Pre-Waste**	**$0.82** *diff. +/-*	**$0.90** *+10%*	**$1.53** *+87%*	**$1.87** *+129%*

Invisible Waste Cost

But where ApiJect really achieves its cost savings verses 10-dose vials is in reduced wastage. Numerous studies have demonstrated how single-dose formats such as Uniject and 1-dose vials have wastage rates significantly below those of 10-dose vials, which have reached 40% wastage or more in certain scenarios. We use a reasonable assumption of 5% waste levels for single-dose presentations and 25% waste levels for 10-dose glass vials.

13	Waste %	5%	25%	5%	5%
14	Waste Cost	**$0.05**	**$0.29**	**$0.09**	**$0.11**
15	**Total Cost of Delivery** (excludes cost of vaccine)	**$0.87** *diff. +/-*	**$1.18** *+36%*	**$1.62** *+86%*	**$1.98** *+127%*

INTRODUCING APIJECT

ApiJect Offers More Than a Dozen Major Benefits that Improve Outcomes.

From improved safety to expanding access by utilizing front-line healthcare workers, ApiJect can improve outcomes and strengthen healthcare systems across the globe.

The ApiJect prefilled syringe was designed to eradicate unsafe injections given by the world's healthcare systems. But in that process, Marc Koska and his team created an entirely new injection device that can help populations and improve outcomes in a number of ways, including:

Eradicates contaminated Injections: Today, more than 3 million patients (including 1.5 million children) die each year from diseases transmitted by contaminated vials and syringes.[12] ApiJect cannot be reused so it cannot spread disease.

Grows Coverage: ApiJect's lower cost means fixed healthcare budgets can procure more vaccines and medicines. And, its simple design means that, where approved by regulators, community healthcare workers can use an ApiJect to deliver an injection.

Reduced Counterfeits: ApiJect uses BFS manufacturing, which requires real expertise and expensive machines that are not easily purchased by counterfeiters. Official logos can be embossed into the BFS plastic that cannot be scratched off, nor duplicated by counterfeiters.

Less Energy, Less Waste: BFS manufacturing is incredibly efficient, especially when compared to creating glass vials. The result is 85% less energy used in manufacturing an ApiJect prefilled syringe versus a glass vial + syringe, and 75% less industrial waste.[13]

Eliminate Dosage Errors: An ApiJect syringe comes prefilled with the correct dosage amount, reducing much of the preparatory work, as well as eliminating injection errors from incorrect dosage amounts.

Simplifies ID and SC Injections: With standard syringes and glass vials, performing an intradermal (ID) or subcutaneous (SC) injection takes significantly more time and skill than a standard intramuscular (IM) injection. ApiJect simplifies this by pre-affixing the right needle length and gauge to the ApiJect prefilled syringe, making every injection fast and easy.

Doctor and Nurse Labor Savings: As a prefilled syringe, ApiJect cuts down on injection preparation and administration time by as much as 50%.[14] This means doctors and nurses can spend less time administering injections and more time treating other patients.

ApiJect's Mission

ApiJect's mission is to eradicate all unsafe injections given by health professionals, which kill 3+ million people and infect another 20+ million with HIV and other life-altering diseases every year. We plan to achieve that goal by eliminating all standard syringes and multi-dose vials from the world.

INTRODUCING APIJECT

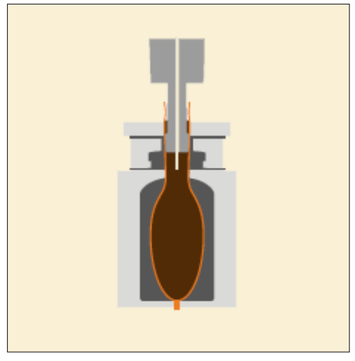
ApiJect has all of the manufacturing advantages of BFS, with the safety of a single-use prefilled syringe.

Adding a leak-proof Needle Hub to a BFS container, a single ApiJect manufact uring line can produce up to 30,000 finished ApiJect prefilled syringes per hour.[15]

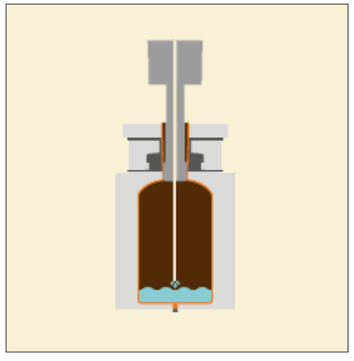
Simply put, an ApiJect prefilled syringe is made by attaching a Needle Hub to a medical-grade BFS plastic container, aseptically filled with the medicine or vaccine.

The Blow-Fill-Seal manufacturing process includes three main steps:

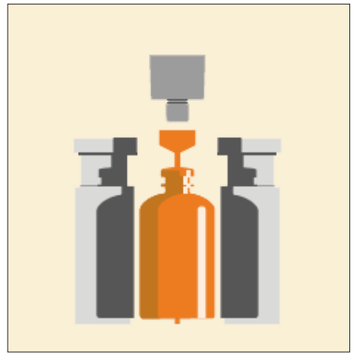
1. Establish supplier & component supplies. First, a pharmaceutical company must decide if they are going to create and fill the BFS container using their own BFS machine, or via a Contract Manufacturing Organization (CMO). The pharmaceutical company then orders Needle Hubs from ApiJect. Each needle hub is made by ApiJect's manufacturing partners to high-quality standards and delivered sterilized to the BFS facility.
2. Manufacture, fill, and seal. In one smooth 3-second process, a BFS machine (a) aseptically creates the container, (b) aseptically fills it with liquid medicine or vaccine, and (c) aseptically seals it.
3. Assemble and Finish: Assembly machines at the BFS facility then attach the Needle Hubs, inspect quality, and finish the ApiJect prefilled syringes for shipping.



a Aseptic Blowing
Positive air pressure creates open space inside parisons. The mold closes (welding shut the parison base) and instantly chills each container to "lock in" its double-bubble syringe shape.



b Aseptic Filling
A mandrel (hollow, needle-like rod) extends into each container. Liquid vaccine or medicine rapidly flows through the mandrel to fill the container with required precise dosage.



c Aseptic Sealing
The mandrel is removed; head mold closes to seal the top of the syringe-shaped container. Excess plastic is then trimmed off ("deflashed").

The ApiJect manufacturing process offers multiple feature options that allow the ApiJect to be tailored for the end customer.

These include:

IM, SC, or ID Needle Size: The customer can choose to have their ApiJects affixed with an intramuscular, subcutaneous, or intradermal needle.

Container Size: BFS containers can be manufactured in an infinite number of shapes. ApiJect has created a standard prefilled syringe shape and size. But a customer can work with ApiJect to customize the shape to their needs, or come up with a completely different design.

Safety Cap: All ApiJects come with a standard safety cap. However, an ApiJect prefilled syringe will work with a range of other safety caps if the customer prefers.

Strip Size: One of the reasons ApiJect prefilled syringes can be produced so efficiently is because they are manufactured in strips. The customer can order ApiJects to be packaged in single units or 5 units in a strip.

Tracking: ApiJect is partnering with Field Tracking Systems to bring dose-level tracking to the point of care. In the future, customers will have the option to add an NFC tag to the label area of every ApiJect. Once touched to a smartphone with the correct app open, the injection event is automatically recorded, appended with GPS and date/time data, and uploaded to the health provider's database for aggregated tracking.

Blow-Fill-Seal (BFS) is a trusted plastic manufacturing process used to package medicines around the world.

Every year, billions of eyedrops, nose sprays, oral vaccine doses, and more are packaged in BFS. This is because BFS is a highly-efficient, low-cost, aseptic filling process. It is also space-efficient; a BFS machine can fit in a shipping container.

Today, there are hundreds of BFS machines in facilities around the world. And with growing sales and R&D spending, BFS is a plastic manufacturing process that more pharma companies should be paying attention to.

INTRODUCING APIJECT

ApiJect can Positively Impact a Wide Range of Challenges and Help Save Millions of Lives.

From injectable contraceptives to pandemic flu, the ApiJect prefilled syringe is a real breakthrough for industries and communities around the world.

The ApiJect prefilled syringe will be effective against a wide range of challenges, including the following:

Global Vaccines & Essential Medicines: ApiJect's low price and ease of use will allow health ministries to cover more people while preventing infections from injections given by health workers.

Injectable Contraceptives: Today, injectable contraceptives are the fastest-growing reversable form of contraception.

ApiJect makes injectable contraception more accessible to tens of millions of women by being so simple that a community healthcare worker can deliver the injection.

Lyophilization and Pets: An ApiJect prefilled syringe can be filled with diluent, making the constitution process for a lyophilized drug much easier.

This is particularly helpful to veterinarians who largely deal with lyophilized vaccines and medicines. (ApiJect is also developing an all-in-one lyophilized injection device.)

Pandemic Defense: A single BFS machine can produce up to 30,000 ApiJect prefilled syringes an hour, enabling governments to have emergency surge capacity in case of a severe flu pandemic or any potentially high-casualty, fast-moving health emergency.[16]

Oxytocin: The WHO estimates that every year, 70,000 mothers in Low- and Middle-Income Countries die from blood loss while giving birth because they are not given an injection of Oxytocin.[17]

ApiJect's low cost and ease of use can help countries and NGOs make sure that Oxytocin is available at all birthing events – whether it is in a hospital/clinic or at a home.

High-Income Hospitals: An easy-to-use prefilled syringe like ApiJect can reduce injection time by 50% or more, enabling nurses to spend less time preparing injections and more time on their other hospital duties.

It will also reduce adverse drug effects by limiting administration and dosage errors.

Established UNICEF and National Suppliers to Provide Global ApiJect Support at Launch.

ApiJect has affiliated with 3 of the largest global syringe manufacturers, as well as BFS leader Rommelag, to provide high-volume, high-quality, low-cost supply. ApiJect's Needle Hub manufacturing partners are located in India, South Korea, and Indonesia.

And in 2021, ApiJect's manufacturing partner Tae-Chang Industrial Co. will open the world's first complete, start-to-finish, ApiJect manufacturing and filling facility.

References and Citations

[1] http://www.who.int/mediacentre/news/releases/2015/injection-safety/en/. Accessed 08/24/18.

[2] www.gavi.org/library/publications/gavi/gavi-2016-2020-mid-term-review-report/ Accessed 12/03/18.

[3] International Pharmaceutical Quality, Sharp Uptick in Recalls for Glass Lamellae Problems Under Scrutiny, Aug 3rd, 2011.

[4] Children's Hospital of Philadelphia, Global Immunization: Worldwide Disease Incidence http://www. chop.edu/centers-programs/vaccine-education-center/global-immunization/diseases-and-vaccines-world-view.

[5] PATH, Reflections on Innovations in Global Health, The Radically Simple Uniject Device.

[6] Path Challenges and Innovations in Vaccine Delivery, 10th Annual African Vaccinology Course (AAVC): Developing Vaccinology Expertise for Africa, 10–14 November 2014 Cape Town, South Africa, by Darin Zehrung, Senior Technical Officer and Portfolio Leader, Delivery Technologies, Vaccine and Pharmaceutical Technologies Group, 13 November 2014.

[7] Ibid. And:
Tiwari, Ranjana & Dwivedi, Shatkratu & Swami, Piyush & Mahore, Rakesh & Tiwari, Sakshi. (2017). A study to assess vaccine wastage in an immunization clinic of tertiary care centre, Gwalior, Madhya Pradesh, India. International Journal of Research in Medical Sciences. 5. 2472. 10.18203/2320-6012.ijrms20172431.
https://www.researchgate.net/publication/317197954_A_study_to_assess_vaccine_wastage_in_an_immunization_clinic_of_tertiary_care_centre_Gwalior_Madhya_Pradesh_India, accessed 08/24/18. And: Vaccine. 2017 Dec 4;35(48 Pt B):6751-6758. doi: 10.1016/j.vaccine.2017.09.082. Epub 2017 Oct 21. https://www.ncbi.nlm.nih.gov/pubmed/29066189. Accessed 08/24/18.

[8] Ibid.

[9] See footnote 3 in ApiJect blue booklet "A better way to inject and track vaccines and medications."

[10] Rommelag Engineering https://www.rommelag-engineering.com/en/info/aseptic-filling/.

[11] See footnote 9.

[12] See footnote 4.

[13] US Energy Information Administration, Glass manufacturing is an energy-intensive industry mainly fueled by natural gas, August 21, 2013.

[14] Claudia C Pereira & David Bishai (2010) Vaccine presentation in the USA: economics of prefilled syringes versus multidose vials for influenza vaccination, Expert Review of Vaccines, 9:11, 1343-1349.

[15] Rommelag Engineering https://www.rommelag-engineering.com/en/bfs/.

[16] Ibid.

[17] World Health Organization, Maternal Mortality Fact Sheet, 16 February 2018 http://www.who.int/en/news-room/fact-sheets/detail/ maternal-mortality.

Other publications available from ApiJect.

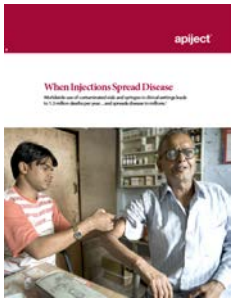
All available digitally at apiject.com/publications.
To request a physical copy, contact info@apiject.com.

How a Low-Cost Mono-Dose Syringe Can Increase Safety and Coverage

Billions of Glass Vials Every Year With Unintended Consequences

Low-Cost Mono-Dose Syringes Enable Many Use Cases for Global Impact

ApiJect's 32 "Soft Benefits" are Difficult to Measure, but Improve Lives in Many Ways



When Injections Spread Disease

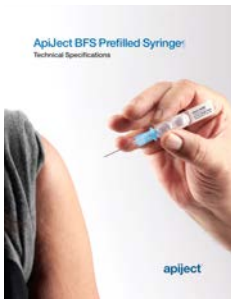
How We Manufacture a Prefilled Syringe with the World's Lowest Cost Per Dose Delivered

Vaccine Technology: Its Past Evolution and Future Landscape

Injectable Contraceptives Not Only Improve the Health and Lives of Women, but Transform Communities

The "Internet of Things" is Already Transforming Health & Medicine

Pet Owners and Small Farms Worldwide Need New and Better Medical Injection Options to Keep Their Animals Healthy



ApiJect BFS Prefilled Syringe Technical Specifications

The Marc Koska Story

apiject™

All available digitally at apiject.com/publications.

For more information, or to request a physical publication, contact us at info@apiject.com. Learn more at ApiJect.com.