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When COVID-19 vaccine and injectable therapeutics become available, the RAPID Consortium can ease a U.S. supply chain problem by filling and finishing 300+ million prefilled syringes per month.

Later, when the pandemic ends, RAPID's prefilled syringe can safely vaccinate millions worldwide who are not vaccinated now...while also enabling remote, real-time injection tracking and reporting.

The COVID-19 pandemic has reminded the U.S. that effective defense against bio-emergencies is multilayered and time-sensitive. This includes developing vaccine and therapeutics, packaging them into individual doses, and eventually injecting hundreds of millions of Americans.

To achieve these critical steps, scientists, government officials and pharmaceutical companies run a “relay race” against time. Most of the focus is on quickly producing vaccines or therapeutics. However, equally vital steps in this relay race occur after millions of doses have been manufactured.

To inject vaccine or therapeutics into America's 330 million citizens, pharmaceutical companies will need to acquire, fill and finish some 130+ million multi-dose glass vials and 660+ million syringes. That's because each citizen may require two injections, 21 days apart, and possibly two additional injections of adjuvant, an immune system booster.⁷ Some of the needed syringes will be used to mix vaccine and adjuvant at the point of care, just prior to injection. The rest will be used to inject the adjuvanted vaccine into subjects.

A major challenge is America's lack of “surge capacity” to quickly produce huge numbers of vials and syringes, which are not stockpiled in large quantities.⁸ Lead times on massive supplies of medical glass vials are at least 6-12 months.⁹ Adequate capacity to “fill and finish” those glass vials is also lacking.¹⁰

Syringes, like glass vials, are also not stockpiled in quantities that could cover the U.S. population more than once. “Just in time” supply chains mean millions of additional units cannot reliably be acquired or manufactured on short notice. Yet another challenge: most medical suppliers are located overseas and may not prioritize U.S. needs.

There is a new way for the U.S. to meet these challenges. For the first time, Blow-Fill-Seal (BFS) plastics manufacturing technology can rapidly produce prefilled syringes in population-scale quantities. By building a network of

relatively small BFS facilities on U.S. soil, the nation will acquire the surge capacity to fill and finish bulk antigen for the entire population in a matter of weeks in a pandemic emergency.

BFS is FDA-approved technology for aseptic mass manufacturing, filling and finishing of plastic containers for various biological liquids. 50 billion BFS plastic bottles a year contain sterile eyedrops, ear drops, nose sprays and certain orally administered vaccines.¹¹ A single BFS machine can produce and fill a container in seconds, manufacturing 30,000 finished units per hour.

BFS can now make prefilled syringes the same way, with equally high speeds and volumes. Simply stated, a Pen-Needle Hub is affixed to each BFS Container as part of the basic manufacturing process.

A new company called ApiJect Systems Corp. has been founded to manufacture the BFS prefilled syringe, known as the ApiJect System. Behind ApiJect stand two of the world's most successful inventors.

Global public health activist and leading medical device innovator Marc Koska, ApiJect's developer, has saved 12 million lives to date with his earlier K1 Auto-Disable syringe design. For this Mr. Koska was made an Officer of the Order of the British Empire.

ApiJect's Chairman and business leader is Jay Walker, one of the world's most successful entrepreneurs, who founded three companies that grew from zero to 50 million customers each. Mr. Walker is also Director of TEDMED, the health and medicine edition of the famous TED conference.

The U.S. government has recognized that BFS prefilled syringes can strengthen America's supply chain for injectable medicine and vaccine in a pandemic or other bio-emergency. Accordingly, the U.S. has formed RAPID, the Consortium for “Rapid Aseptic Packaging of Injectible Drugs.” RAPID



will build and operate a BFS production network for prefilled syringes on U.S. soil under a public-private partnership that combines government agencies, ApiJect, and other private industry concerns.

RAPID's government partners include the U.S. Department of Health and Human Services (HHS), specifically the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR), and the Strategic National Stockpile.

RAPID will raise \$500 million to \$1 billion in private capital to fund construction of BFS manufacturing facilities within the U.S. over the next few years, capable of producing 330 million ApiJect prefilled syringes per month — enough to cover the entire U.S. population.

A vital RAPID capability will be remote, real-time tracking of ApiJect injections in the field, enabled by an NFC (Near Field Communication) tag, affixed to each BFS prefilled syringe. Just before injection, a health worker taps the NFC tag to their smartphone (just like using Apple Pay at a checkout counter).

A free mobile app will capture and automatically upload the tag's unique, encrypted serial number. It will also append patient-anonymous data (time, date, GPS location, etc.) to the government's designated cloud database. Data can be aggregated and analyzed to provide real-time coverage maps for more efficient vaccination campaigns.

Meanwhile, with the spread of COVID-19, the U.S. needs population-scale injection capacity starting this year, to cover all citizens with therapeutics as soon as they become available. Accordingly, RAPID is developing "Project Jumpstart" to provide this capability by late 2020. Under "Jumpstart," the ApiJect BFS prefilled syringe can be manufactured in existing domestic BFS facilities, converted to immediate pandemic defense under a long-term lease.

Jumpstart's BFS prefilled syringe will consist of the BFS Container and a separate Needle Hub, shipped together and activated for injection at the point of care by a simple push-twist motion that assembles the two components.

With longer-term vaccine packaging capacity and short-term therapeutics packaging capacity, RAPID will strengthen a vital link in the chain of U.S. pandemic preparedness and biodefense.

When the crisis passes and the U.S. no longer requires immediate vaccination or treatment of 330 million people, the RAPID network can be economically self-sustaining

by performing commercial work.

Separately, when ApiJect's BFS prefilled syringe is not needed in high volumes for pandemic defense, it can play a valuable role in promoting improved global health. Overseas health ministries and global health organizations can deploy ApiJect to bring vaccines to more people, including the 14% of the world's children who are not currently vaccinated against routine childhood diseases.⁶

While expanding global vaccination coverage, ApiJect can also increase safety, reduce healthcare costs for many countries, and help save many of the 1.3 million lives that are lost each year due to contaminated medical injections.

Safety is increased because the ApiJect BFS prefilled syringe is an Auto-Disable, single-use device. Since it cannot be reused, it cannot spread disease from one patient to the next. In addition, since a prefilled syringe requires no filling from a glass vial, there is no chance of contaminating vial contents — currently a major cause of many unsafe injections and resulting fatalities.

Healthcare costs are reduced by ApiJect because prefilled BFS syringes enable vaccine injections at a lower cost per dose delivered than today's lowest-priced format, a 10-dose vial and 10 disposable syringes. National health ministries in Low- and Middle-Income Countries that have been using 10-dose vials can now afford to switch to BFS prefilled syringes, increasing safety with no reduction in population coverage.

In addition, while rules will vary by country, regulators may authorize ApiJect injections by community health workers in addition to medical professionals. For example, in low-resource countries, ApiJect could potentially be used to administer Oxytocin to new mothers and the birth dose of Hep-B. It could also support discreet self-injection of contraceptives, supporting wider use. And, ApiJect could deliver the forthcoming new HIV therapeutic, as well as regular anti-malarial injections.

The world will always face enormous health challenges — both during emergencies like pandemics, and in ordinary times when millions risk disease and mortality from lack of access to injectable medicines and vaccines, or from unsafe medical injections. Fortunately, RAPID and the ApiJect BFS prefilled syringe are now available to address both bio-emergencies and ongoing global health needs in a way that protects more Americans, faster, and offers greater global access, equity and safety for basic care.

The World's First BFS Prefilled Syringe

*Better delivery of injectable vaccines and medicines.
Faster pandemic response. Stronger global health.*

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 **RAPID** USA

**“Vaccines don’t save lives;
vaccinations do.”**

— Dr. Walt Orenstein,
Director of the CDC’s
U.S. National Immunization Project, 1993-2004¹⁶⁷

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RAPID USA

Dear Colleague,

Few things provide clarity like a crisis. As the world unites against the COVID-19 pandemic, two things are becoming increasingly clear.

First, effective pandemic defense requires providing entire populations with injectable therapeutics and vaccines, ideally as soon as they are approved by regulators and manufactured in bulk. Second, this objective will be difficult to achieve using traditional glass vials and syringes.

Supply chains for both products are largely offshore. With “just in time” manufacturing, stockpiles are minimal; lead times from orders to initial deliveries often run six months or more. Temperature-controlled, bio-safe facilities for filling glass vials with vaccine are already operating at capacity, mostly offshore.

We believe there is a better way to provide injectable therapeutics and vaccines in individual doses — a way that will strongly support U.S. and global efforts to mount an effective pandemic defense. Aligned with the World Health Organization’s goals for health systems strengthening, we have developed the ApiJect System: a single-use, prefilled syringe that can be manufactured at population scale, at unprecedented high speed.

Our BFS prefilled syringe is manufactured with a proven high-speed aseptic packaging technology called Blow-Fill-Seal (BFS). A Needle Hub comes with each preloaded BFS container for push-twist assembly and activation at the point of care, just before injection.

We seek regulatory approval and mass production launch by yearend — or sooner — through The RAPID Consortium, a public-private partnership between the U.S. Government, ApiJect Systems Corp. and other commercial organizations.

A network of 30 BFS manufacturing lines, housed in several dedicated, onshore facilities, could produce 330+ million BFS prefilled syringes per

(continued ->)

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month, which is more than enough to cover the entire U.S. population. If a second injection is needed 21 days later — often the case for a new vaccine — and if an adjuvant (immune system booster) must be mixed with the vaccine at the point of care, requiring the use of additional “mixing syringes,” then BFS technology and RAPID can meet those needs as well.

The ApiJect BFS prefilled syringe was originally developed to enable Low- and Middle-Income Countries to economically vaccinate more of their populations. Cost per dose delivered with BFS prefilled syringes is significantly lower than the current lowest-cost format (10-dose vial with disposable syringes). Our low cost will support global health efforts targeting, among others, 14 million children a year who go unvaccinated now. And, as a single-use platform that requires no glass vials, the BFS prefilled syringe is a safer choice, too. It cannot be reused, contaminated, or spread disease.

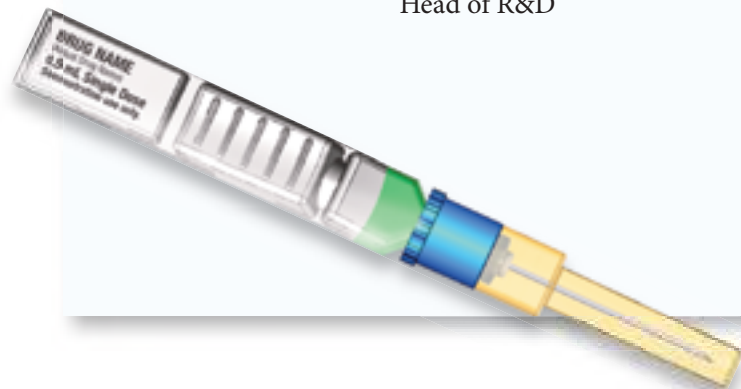
Data technology makes the BFS prefilled syringe even more effective in combating pandemics and promoting routine vaccinations. A 5-cent digital chip on each ApiJect System communicates with the health worker’s mobile phone at the time of injection, automatically generating a real-time, GPS-based usage report to the global health network. Aggregating injection data enables comprehensive, up-to-the-minute tracking of vaccination campaigns.

As the inventor of the BFS prefilled syringe and the leader of its technology and business activities respectively, we are excited to share our vision. We invite you to join with us as we work to deliver an important advance in pandemic defense and global health that can benefit everyone, everywhere.



Marc Koska
Inventor
Head of R&D

Jay Walker
Chairman
ApiJect



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“Containing a pandemic will require an end-to-end solution...Supply chain issues are among the most significant challenges to preparing for an influenza pandemic as well as other infectious diseases.”¹⁹⁸

**— Robert Kadlec, MD, MTM&H, MS
Assistant Secretary For Preparedness and Response
U.S. Department of Health and Human Services**

STRENGTHENING PANDEMIC PREPAREDNESS

SECTION 1

**Strengthening Pandemic Preparedness
with BFS Prefilled Syringes**



**Successful vaccination in a pandemic
depends on 12 linked, sequential steps.**

**Critical links in the supply chain are broken.
But now we can bridge the gap.**

Pandemic vaccine production and deployment is a 12-PA RT RELAY RACE against time, with stakes of life or death.

In an influenza pandemic, the pathogen spreads rapidly but vaccine R&D and packaging requirements are time-consuming. If we drop the baton at any one of the 12 stages, the cost is very high in both human lives and economic terms.



STRENGTHENING PANDEMIC PREPAREDNESS

Despite vaccines, seasonal flu annually infects 1 billion and kills up to 650,000 people worldwide.¹⁶⁹

Much of the public thinks of “the flu” as merely a nuisance. But all too often, it is fatal.

Influenza (flu) is a contagious respiratory illness caused by viruses that infect the nose, throat, and sometimes the lungs. The illness can be mild – a few days of coughing, aches and fever – or it can lead to hospitalization and even death. Up to 11% of the U.S. public contracts influenza in any given year, according to the U.S. Centers for Disease Control and Prevention (CDC).¹⁷⁰ Many strains of seasonal influenza virus exist, and they are

constantly evolving, sometimes mutating through multiple generations in a single year. Influenza viruses circulate in different times in different places around the world. In temperate regions, such as the U.S. and the rest of the northern hemisphere, influenza epidemics occur in late fall and winter. In contrast, influenza circulates most frequently in the southern hemisphere from May to September, so the world as a whole has two “flu seasons” in each calendar year.¹⁷²

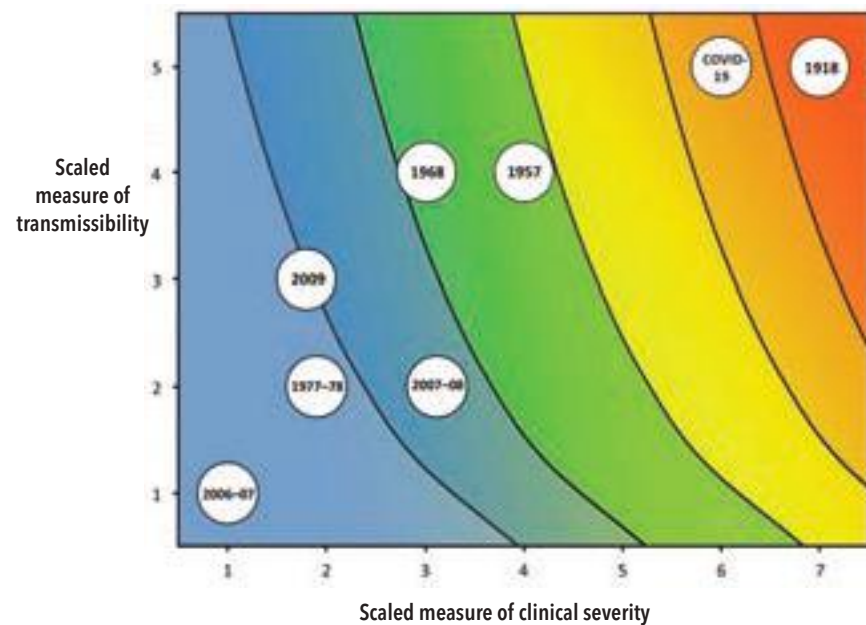
Even though the typical virus that drives seasonal flu is constantly changing, it is usually one that is closely related to a strain that has recently circulated. But at unpredictable intervals, a new strain of influenza emerges, creating a novel and unpredictable strain that humans have never faced before.

The result can be a pandemic, a potential global health crisis which the World Health Organization describes this way:

“An influenza pandemic occurs when a new influenza virus emerges and spreads around the world, causing large numbers of illness and deaths, as most people will not have immunity to the new virus. Influenza pandemics can be mild, moderate or severe.”¹⁷³

When pandemics occur, they move through a population in waves, with the numbers of cases cresting and ebbing two or three times before the pandemic ends.

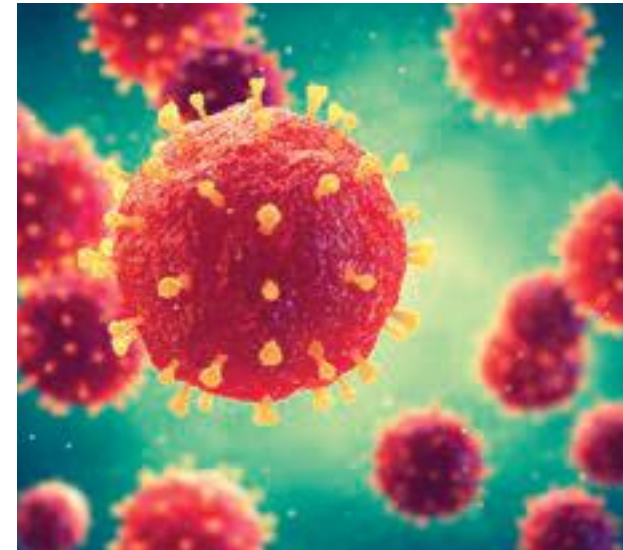
**Pandemic Severity Assessment Framework (PSAF):
Pandemic Influenza and Epidemic Influenza Severity¹⁷¹**



Source: Institute for Disease Modeling, Feb. 29, 2020, adapted from: Reed C, Biggerstaff M, Finelli J, Koonin LM, et al. Novel framework for assessing epidemiologic effect of influenza epidemics and pandemics. *Emerg Infect Dis* 2013;19(1): 85-91.

STRENGTHENING PANDEMIC PREPAREDNESS

The global strategy for combatting seasonal flu is also the basis for containing a pandemic.



“Seasonal and pandemic flu preparedness are closely linked, given that vaccine production for seasonal flu viruses is the foundation for vaccines production for a pandemic flu,” according to a September 2019 report by the U.S. Council of Economic Advisers (CEA).¹⁷⁴

The process of creating seasonal flu vaccine begins six months before flu season begins, based on predictions by scientists regarding which flu strains will pose the greatest threat. This predictive approach is not feasible for producing a pandemic-specific vaccine. Scientists don't know when a new pandemic will emerge or which new type of influenza virus will cause it. That means a vaccine for a pandemic virus cannot be produced until after a pandemic arises. Therefore, ongoing surveillance and laboratory research is critical to identifying the

emergence of any novel influenza virus that may have pandemic potential. Although systems in the U.S. can rapidly assess the emergence of new influenza viruses, the disease will likely be circulating through the human population in multiple countries and perhaps worldwide.

“The main method of producing [seasonal] flu vaccines currently in use relies on production in chicken eggs and takes six months or more to produce adequate doses of vaccine [for population-wide coverage],” explained the CEA, which cited WHO when it added: “Essentially, the same 6-month, egg-based process is used to make vaccines in the case of pandemics.”¹⁷⁵

Accordingly, any vaccine intended to combat a large-scale pandemic during the first wave of disease spread “would arrive too late to avert a meaningful number of infections and deaths,” according to that same CEA report.¹⁷⁶

STRENGTHENING PANDEMIC PREPAREDNESS

A pandemic spreads to many people before a new vaccine can be developed, manufactured and distributed.



Scientists may detect a new U.S. outbreak as soon as 1 week after it starts.

Once the virus is detected and analyzed by U.S. and other scientists, and then officially declared to be a pandemic by the WHO, next comes emergency declarations from the U.S. Secretary of Health and Human Services and by the President of the U.S. After that, scientists begin working around the clock to develop a vaccine for the pandemic.

Vaccine development and production move with impressive speed when compared to the typical 18-year process that is required for new drug R&D and U.S. government and FDA approval.

However, that same vaccine production timeline is relatively slow in comparison with a quick-moving influenza virus, where cases can pop up nationwide in

weeks or even days. The flu virus spreads quickly.

According to WHO, "It takes approximately five to six months for the first supplies of approved vaccine to become available once a new strain of influenza virus with pandemic potential is identified and isolated."¹⁷⁷

Growing the virus in eggs is also slow and difficult for various technical reasons, and because of a number of manufacturing bottlenecks.

Once vaccine becomes available, it will be important to swiftly vaccinate as many people as possible. Unfortunately, patients can't simply take the vaccine in pill form because digestion destroys the vaccine.

Effective vaccination requires direct injection into each person. This requires skilled administrators to give the injections, as well as other logistical requirements.

STRENGTHENING PANDEMIC PREPAREDNESS

The U.S. would need up to 130 million 10-dose vials for vaccine and adjuvant, but vials have major drawbacks.



Mono-dose glass vials are the U.S. standard, but to cover the entire population in a pandemic, vaccine may need to be packaged in 10-dose glass vials. This format comes with several significant disadvantages.

The U.S. Department of Health and Human Services (HHS) maintains a National Pre-Pandemic Influenza Vaccine Stockpile containing bulk vaccine made from novel influenza viruses with "pandemic potential."

However, this stockpile does not have tens or hundreds of millions of sterile mono-dose glass vials and syringes on hand, waiting for emergency use. Pharmaceutical manufacturers will be forced to package vaccines in 10-dose glass vials instead.

At first glance, this change of formats may appear to

offer efficiencies and economies of scale. But in fact 10-dose vials have significant disadvantages when compared with mono-dose vials (which are not available in sufficient quantities) and with low-cost prefilled syringes produced with new technology.

First, 10-dose vials require 10-20% overfill of the drug to ensure a sufficient margin of supply. This noticeably increases the overall cost per dose delivered.

Second, this overfill means more of the drug must be manufactured, which adds to the time required to provide population-scale injection coverage.

Third, filling a syringe from a vial and injecting a patient takes significantly longer than using other injection formats, such as prefilled syringes. This can lead to long queues and wait times for vaccinations.

STRENGTHENING PANDEMIC PREPAREDNESS

The U.S. must rapidly fill at least 66 million 10-dose vials, and then finish them — but capacity is limited.



Fill & finish operations are typically performed at dedicated, privately-owned facilities.

The U.S. has domestic fill-finish capacity “on reserve,” but not enough to ensure multiple injections for each citizen in a short time.

Once sufficient quantities of a vaccine and the needed vials become available, the vials must be repeatedly washed and sterilized, filled with the correct volume of vaccine, sealed with a rubber stopper and crimp, labeled, serialized, wrapped and boxed.

Even without a pandemic or other bio-emergency and a surge of demand for emergency services, this stage of the medical supply chain already creates a significant bottleneck for pharmaceutical companies attempting to get their current products to market.¹⁷⁹ Like glass

manufacturing, filling vials with vaccine or medicine, then finishing them, requires a time-consuming process. What’s more, most filling lines are not set up or qualified to handle biologics.

Questions over the sufficiency of available fill-finish capacity have long been a concern for the HHS Assistant Secretary for Preparedness and Response.¹⁸⁰ Although the U.S. has currently arranged for a few domestic companies to fill and finish enough 10-dose glass vials for each citizen to receive a single injection, multiple injections may be required for robust pandemic defense — in which case, U.S. capacity for speedy fill-finish operations may be stretched to the limit or beyond. This vulnerability has been identified by the World Health Organization as a significant potential bottleneck in population-scale vaccine delivery.¹⁸¹

STRENGTHENING PANDEMIC PREPAREDNESS

In a severe pandemic, we’ll need single-use plastic disposable syringes for at least 660 million injections.



In a pandemic, people will probably need two vaccinations for full protection, plus additional syringes to mix vaccine and adjuvant. The U.S. lacks enough syringes for this and cannot acquire them quickly.

According to Dr. Robert Kadlec, the HHS Assistant Secretary For Preparedness and Response, “The U.S. lacks sufficient domestic manufacturing capacity and/or raw materials for almost all pandemic influenza medical countermeasures, including vaccines and therapeutics, [and] the needles and syringes needed to administer them...”¹⁸⁴ This shortfall applies to all pandemics.

Syringe shortages can occur when the system is stressed. In September of 2017, Hurricane Maria struck Puerto Rico, home to the major factories that supply U.S. hospitals with saline bags (containers for intravenous injections of sterile saline). When these facilities were

shut down by wind, water and power failures, shipments of saline bags to U.S. hospitals came to a halt. As a result, these hospitals quickly ran through their limited local inventories of saline bags. Medical staff began using syringes to inject saline into patients. But then, hospitals began running out of syringes.¹⁸²

The U.S. government owns no syringe manufacturing facilities; has no surge capacity for rapid production of syringes at scale; and depends on commercial facilities where “just in time” production is already fully committed to private customers under contract.

In the face of a potential mass outbreak, federal officials might have to invoke the Defense Production Act to press America’s private industry into service on behalf of the nation’s health.¹⁸³ But most syringe manufacturers are located abroad and not subject to the requirements of the law.

“The U.S. lacks sufficient domestic manufacturing capacity and/or raw materials for almost all pandemic influenza medical countermeasures, including vaccines and therapeutics, the needles and syringes needed to administer them, and personal protective equipment, including masks, needles, and syringes.

“Further, in a pandemic, global manufacturing capacity will likely not be sufficient to meet demand, resulting in an inability to import adequate quantities of medical countermeasures.”¹⁸⁴

**— Robert Kadlec, MD, MTM&H, MS
Assistant Secretary For Preparedness and Response
U.S. Department of Health and Human Services**

STRENGTHENING THE U.S. SUPPLY CHAIN

SECTION 2

**We Will Strengthen
the U.S. Pandemic Supply Chain**



A well-accepted, regulatory-approved technology called Blow-Fill-Seal will provide rapid “surge capacity” for prefilled syringe production and fill-finish operations.

Using this technology, our public-private partnership will build the capacity to make 330 million prefilled syringes per month once the bulk vaccine is available for packaging.

STRENGTHENING THE U.S. SUPPLY CHAIN

The new Consortium for Rapid Aseptic Packaging of Injectable Drugs (RAPID) will provide fast U.S.-based capacity to aseptically manufacture up to 330,000,000 sterile, prefilled syringes every month.

As a public-private partnership, the Consortium for the Rapid Aseptic Packaging of Injectable Drugs will build and operate 30 cold-chain production lines inside several U.S.-based facilities.

A public-private partnership of U.S. agencies, commercial enterprises, and private funders are coming together to create a consortium to build and operate a network of BFS fill-finish facilities.

The fill-finish shortfall facing the U.S. today leaves the population vulnerable to a severe pandemic.

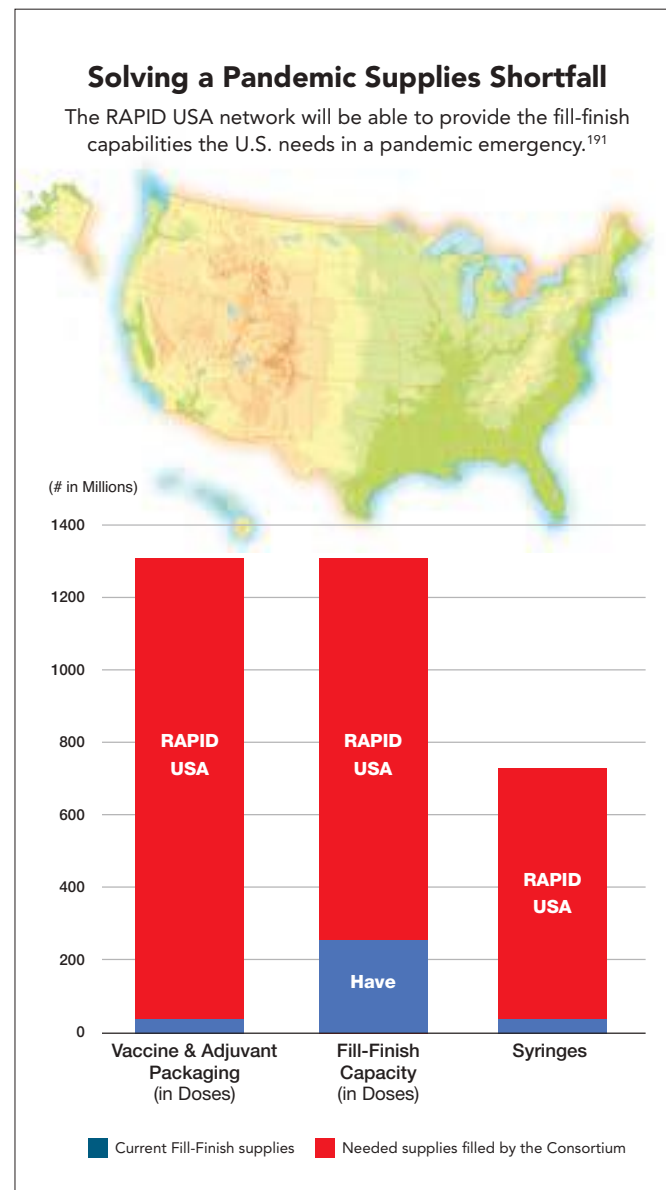
The ability to create prefilled syringes from Blow-Fill-Seal (BFS) plastic manufacturing technology will allow the U.S. government to defend its population quickly and efficiently when a severe pandemic or other biological threat emerges.

That is why the Office of the Assistant Secretary for Preparedness and Response, the Strategic National Stockpile, and other U.S. agencies are forming a public-private partnership with ApiJect and high net-worth private funders to build the Consortium for the Rapid Aseptic Packaging of Injectable Drugs (RAPID).

The Consortium's network of BFS facilities, called RAPID USA, located on U.S. soil, will allow for the production of 330+ million prefilled syringes per month in the event of an emergency.

Together, members of the Consortium will do the needed R&D, build the network, and manage its operations to produce continuous commercial work so that pandemic defense is always ready when needed.

In the short term, RAPID USA can help combat the coronavirus by quickly establishing the capability for domestically manufactured BFS prefilled syringes using existing U.S.-based BFS facilities (see page 22).



BFS technology will rapidly create the 660+ million prefilled syringes needed to give each U.S. citizen 2 injections in a pandemic.



Using BFS prefilled syringes replaces steps 5-7 and part of step 8 in the current 12-step process for pandemic defense. This allows for far faster response times once drugs and therapies are available.

Each facility will use Blow-Fill-Seal (BFS) manufacturing for rapid scale-up, low unit costs and high safety levels.

BFS-enabled prefilled syringes offer many advantages over traditional syringes and multi-dose glass vials, including:

1. Rapid, population-scale manufacturing.
2. BFS is temperature-friendly for filling "heat-sensitive" vaccines and/or adjuvants.
3. No separate sterilization needed.
4. No glass vial stockpiles needed.
5. No 6-month lead times for new, emergency glass vial production.
6. Very high reliability: at least 70% uptime.
7. Low-cost adaptability and customization of all plastic elements.
8. Single-use disposable syringe format prevents cross-contamination.
9. Faster to inject (no syringe filling from separate glass vials is required).
10. Integrated anti-counterfeiting security mark option. Also, optional NFC chip.

STRENGTHENING THE U.S. SUPPLY CHAIN

Manufacturing, fill-finish and supply chain problems will be reduced with a new syringe design and dedicated sites.

U.S.-based facilities that prioritize pandemic response will produce up to 20 million prefilled syringes per month per machine starting within hours of bulk delivery of the liquid vaccine.

The necessary technology does exist. It is a proven, well-established plastics manufacturing process called Blow-Fill-Seal (BFS), combined with a familiar type of component called a Needle Hub that enables needles to be attached to plastic “squeeze-bubble” type containers.

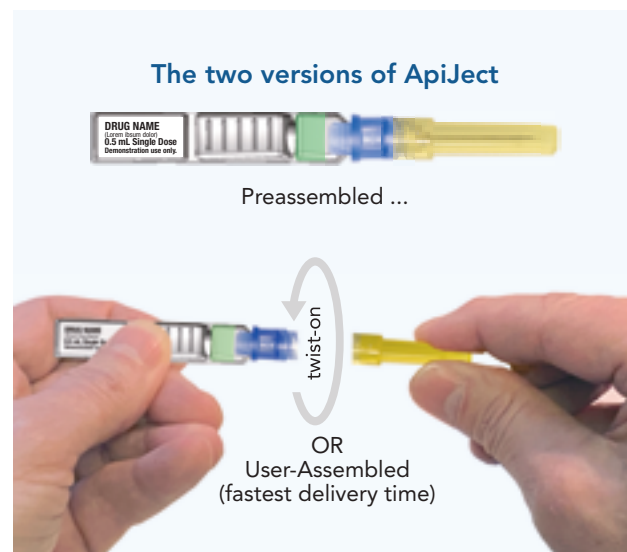
The result is a new type of prefilled, single-dose, one-use syringe that can be produced in extremely high numbers, and with extreme speed. A single BFS machine, roughly the size of a truck, can produce up to 20 million FDA-approvable finished doses per month, packaged in prefilled syringes and ready to ship starting within 4 hours of receiving bulk antigen and adjuvant.

An “injection readiness network” with just a couple dozen machines in domestically located facilities could rapidly and reliably produce a combined total up to 330 million prefilled syringes per month.

Built and operated by RAPID USA, this nationwide network of BFS facilities will give emergency vaccine production top priority. Production lines will be used for commercial or military preparedness manufacturing when not needed to combat pandemics or to meet other biodefense challenges. But in the event that a severe pandemic occurred, federal health officials will have the authority to immediately switch any or all of the facilities in the network to manufacturing of prefilled syringes containing the necessary vaccine.



BFS machines are compact. This allows 6-8 machines in a 100,000 sq. foot facility to produce a billion sterile BFS doses a year.



ApiJect devices can be preassembled or assembled in the field from 2 twist-lock components (much like a standard luer lock or luer slip).

STRENGTHENING THE U.S. SUPPLY CHAIN

Blow-Fill-Seal (BFS) is an FDA-approved technology to manufacture, fill and finish sterile drug containers.¹⁸⁵



BFS has aseptically packaged billions of eyedrops, oral vaccines and other drugs... but never in a ready-to-go prefilled syringe format.

BFS technology has been approved by the FDA, EMA, WHO and by health regulatory agencies worldwide.

Around the world, BFS technology is currently used to manufacture 50 billion low-cost plastic “squeeze-bottle” containers every year. Contents include sterile eyedrops, eardrops and nasal sprays as well as a limited number of oral vaccines.¹⁸⁶ BFS technology can safely package most liquid biologicals, including vaccines that are suitable for medical countermeasures.

A low-heat sealing process enables almost any drug or vaccine to be aseptically filled. Medical-grade plastics

are used, specifically well-understood types of TPE (Thermoplastic Elastomer) and PP (Polypropylene).

The result is a prefilled syringe with a validated shelf life of 2-3 years. In some cases, 10-year shelf life is possible. Medical-grade plastics, produced with BFS technology, are the modern alternative to glass.

The FDA has acknowledged since 2004 that BFS confers definite advantages for medicinal delivery.

The agency’s 2004 publication, “Guidance for Industry – Sterile Drug Products Produced by Aseptic Processing,” remains its current statement on BFS standards. That document notes: “Advantages of BFS processing...include rapid reservoir closure processing and minimized aseptic interventions.”¹⁸⁷

STRENGTHENING THE U.S. SUPPLY CHAIN

BFS manufacturing allows for unplanned system startup with very short lead times...and very fast surge scale-up.



From manufacturing line startup to full-speed finished goods output typically takes just a few hours and allows for separate daily batch runs.

Speed and scale are hallmarks of BFS manufacturing. Every facility operated by the Consortium will be capable of switching over active production lines on an emergency basis within just 4 hours of receiving a shipment of pharmaceuticals for packaging. From manufacturing line startup to full-speed finished goods output typically takes just 1-2 hours.

A single machine is capable of producing 500 prefilled syringes every minute, filled, finished, sterilized and ready to ship... which is 30,000 syringes per hour... 20 million per month. And, that's the output from just one small-footprint machine. Across the network, collective production capacity will exceed 330 million

finished, prefilled syringes per month. This is more than double our current fill-finish surge response capabilities.

With production lines located wherever federal health authorities believe would be most advantageous, the BFS facilities will maintain a total stockpile of 660 million needles and an appropriate number of Needle Hubs, as well as bulk plastic supplies, injection molding machines (to make Needle Hubs on site) and fully redundant backup components such as spare molds and parts.

Facility operations will include vaccine, medicine and adjuvant container manufacturing; aseptic filling at low heat; container sealing; needle attachment; sterilization; leak testing; optical inspection; labeling; temperature monitor application; serialization; vapor-wrapping; box packaging; box labeling/serialization; cold chain storage and automated skid packaging.

STRENGTHENING THE U.S. SUPPLY CHAIN

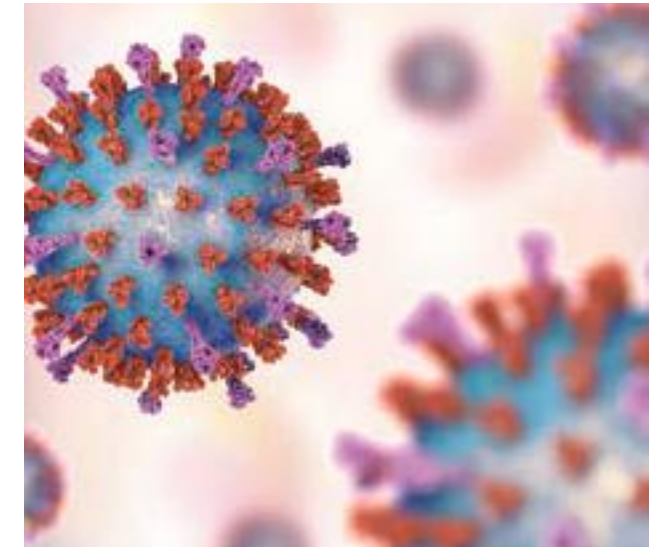
Pandemic vaccine may need to be mixed with an “adjuvant” (immunity booster) at the time of injection.

As defined by the CDC, an adjuvant is “an ingredient (such as certain aluminum salts) used in some vaccines that helps create a stronger immune response in people receiving the vaccine.”¹⁸⁸

Once the novel influenza virus causing the pandemic is identified, and a matching vaccine is in production, scientists will determine if an adjuvant is needed and if so, which one will be most effective. In some cases, adjuvant must not be pre-mixed with pandemic vaccine, requiring separate shipment in multi-dose containers.

At the point of care, if traditional vial-and-syringe technology is used, the administrator of the vaccine will mix the adjuvant with the vaccine just prior to giving each injection. This requires many more glass vials and significantly more syringes than a non-adjuvanted vaccine. It also requires many more fill-and-finish operations.

BFS prefilled syringes will eliminate the need for glass vials for both vaccine and adjuvant, and eliminate the need for additional syringes to withdraw adjuvant for mixing with vaccine. If adjuvant and vaccine can be pre-mixed during fill-and-finish production (like adjuvanted



vaccine that protects against seasonal influenza), the BFS facilities will prefill syringes with the precise mixture. If adjuvant and vaccine must be mixed at the point of care, a dual-chamber variation on the basic BFS design will contain vaccine in the first sealed chamber, and adjuvant in a separate, second chamber. Squeezing the top air bubbles pushes vaccine and adjuvant into a (third) mixing chamber, then through the needle into the patient.



STRENGTHENING THE U.S. SUPPLY CHAIN

The RAPID USA network will provide population-scale capability for multiple injections as soon as this year.

The Consortium for Rapid Aseptic Packaging of Injectable Drugs, overseen by a public benefit corporation, will bolster U.S. pandemic defense.

“[Pandemic preparedness] is like a chain—one weak link and the whole thing falls apart,” according to one of the U.S. government’s most experienced health scientists. “You need no weak links.”¹⁹⁰

As a public-private partnership, and now that the U.S. government has joined the Consortium, RAPID USA is raising private capital and will begin construction on the first facility in 2020. Meanwhile, with the rise of coronavirus and the spread of COVID-19, the U.S. may need population-scale injection capacity on an emergency basis — starting this year — to cover all citizens with therapeutics as soon as they become available.

Accordingly, RAPID USA is developing “Project Jumpstart,” which by late 2020 will provide this capability. Under “Jumpstart,” RAPID will produce a two-part, user-assembled version of its BFS prefilled syringe that can be manufactured using existing domestic BFS facilities, secured for immediate conversion to pandemic defense under a long-term lease. The two-part BFS prefilled syringe will consist of the BFS container and a separate Needle Hub, shipped together and activated for injection at the point of care by a simple push-twist motion that combines the two components.

With long-term vaccine packaging capacity and short-term therapeutics packaging capacity, RAPID will strengthen a vital link in the chain of U.S. pandemic preparedness and biodefense.



SAFE MEDICAL INJECTIONS

SECTION 3

Unsafe Medical Injections Cost 1+ Million Lives a Year



Improperly reused syringes and contaminated multi-dose vials spread disease.

Worldwide, 80% of all vaccines are distributed in multi-dose vials.

SAFE MEDICAL INJECTIONS

How One Man's Vision Helped Spark a Global Revolution for Safe Injections

Marc Koska took on a challenge that everyone believed was impossible. He helped save millions of lives...and helped transform the world of medical injections.

How does someone who is not a credentialed scientist, not a licensed medical professional, an industrialist or technology wizard play a leading role in changing the world's medical practice...helping to save millions of lives?

Marc Koska claims he did it by sheer perseverance.

Those who know him best say the secret was also passion and courage – plus a rare instinct for practical engineering.

In the mid-1980s, the world was just awakening to the threat of HIV-AIDS. Marc, a forensics evidence expert, was shocked to learn that likely half of all future HIV transmissions would come from reused, contaminated syringes, often in healthcare settings.

Equally shocking, these same syringes kill at least 1.3 million people a year by spreading HIV and other diseases.¹⁶⁴



Marc added his voice to those of WHO, PATH, Gavi and others, whose leaders were calling for universal adoption of Auto-Disable (AD) syringes – injection devices that can only be used once. Since they cannot be reused, they cannot spread disease. Marc also designed an AD syringe himself, the K1. The K1 was special because it could be manufactured on modified, existing equipment, making it the world's lowest-cost AD syringe.

In 2001 UNICEF, the world's largest vaccine buyer, became the K1's first customer. Over the next decade, the K1 sold 8 billion units and helped to save an estimated 10 million lives. In recognition of his contribution, Marc was named an Officer of the Order of the British Empire.

By the early 2010s, vaccines were increasingly delivered with AD devices. Yet the majority of medicinal injections today are still given with disposable (reusable) syringes, filled from multi-dose glass vials that often become contaminated by one or more reused syringes.

Why is this high-risk equipment still used today in more than 100 low- and middle-income countries?

The answer is cost. Disposable syringes and glass vials are the lowest-cost option...and in many countries, cost is the overriding factor. Buying the lowest-cost injection system translates into serving the most possible patients.

Still, why do so many health workers in these countries insist on reusing syringes? Why risk contaminating the contents of the glass vials that fill those syringes?



Simply put, in low-resource settings, there is strong economic pressure to reuse any equipment that appears safe and in good working order. Health workers in these countries often believe that washing a used syringe in alcohol, or in boiling water, decontaminates it. This is not the case, but unfortunately no amount of training deters many of these well-meaning health workers from what WHO calls an “ingrained” practice.

Upon learning this, Marc – like other leaders in the field of injection safety – had a startling realization. To save lives from unsafe injections, it would not be sufficient to eliminate all traditional (non-prefilled) syringes. It would also be necessary to eliminate the multi-dose glass vials from which traditional syringes are filled.


This new challenge was largely economic. Any replacement technology for injections had to cost less than traditional vials and syringes. Otherwise, it would not be adopted at scale in low-resource countries. Patients would continue dying from unsafe injections.

Marc began seeking ultra-low-cost methods and materials that could help him revolutionize all injections, not just vaccinations, by producing a prefilled, single-use device

that would replace both vials and syringes with a truly new lowest-cost option. Eventually, he found an extraordinarily fast, low-cost technology called Blow-Fill-Seal (BFS) plastics manufacturing. It's the same technology used to manufacture 50 billion sterile containers a year of eye drops, nose sprays, eardrops and the like. Putting his engineering skills to work, Marc designed a hub that attaches the same needle already used on syringes to a BFS “squeeze-bubble” container. It is a revolution for BFS.

The result is the ApiJect System, featuring a new “soft” syringe with pre-attached Needle Hub that can be configured with all standard needle sizes. It will be the lowest-cost delivery system available for both vaccines and medicines. It will work with local cultures, not against them; and with limited healthcare budgets, not against them.

Marc Koska believes he has developed an innovative solution that the medical world desperately needs. Based on early signs of support from important organizations in global healthcare, he may be right.

 To learn more about Marc's crusade against iatrogenic infections from health care workers, please visit themarckoskastory.com.

SAFE MEDICAL INJECTIONS

A 165-Year-Old Technology Won't Get Us Where We Need to Go

Glass vials and disposable syringes have let us reach 86% of the world. To safely reach 100%, including the poorest, we need a new approach.

The world has achieved astounding progress in global health over the past 100 years.

Billions of medical injections are given each year, saving countless lives.⁴ Of these injections, about 5% are vaccines at an estimated cost of \$50 billion per year.⁵ According to Gavi and WHO, 86% of the world's children are now immunized with one or more vaccines.⁶ For science, it's one of the great accomplishments of the last 100 years...and the global health community is working hard to finish the job. There are three critical remaining challenges.

The 3 challenges of global injections:

- **Coverage:** If one in eight of the world's 1.9 billion children (12%) are not fully vaccinated, as reported by Gavi, then over 160 million children need coverage.⁷
- **Fairness and equity:** Millions of children, mothers and patients do not have access to vaccines and medicines – especially in low-income areas.⁸
- **Safety:** A large, but unknown number of people each year, often among the poorest, are infected with diseases via injections from reused disposable syringes and contaminated multi-dose vials.⁹

The common factor shared by all three problems is the world's reliance on multi-dose glass vials and disposable hypodermic syringes.

Since the introduction of hypodermic syringes in the 1850s, this technology has enabled nurses, paramedics and doctors to give trillions of injections to patients with



acceptable levels of reliability, safety and cost.¹⁰ Still, the three challenges persist, despite the world's best efforts to solve them...and despite billions invested in possible solutions. The last 12% is a hard nut to crack.

Surprisingly, the root of the problem isn't a lack of funds or a shortage of vaccines or medicines. The root of the problem is that the glass vial-and-syringe system has become antiquated. It now imposes a dozen legacy drawbacks – including inefficiency, waste, inaccurate dosage, incorrect usage, and slow administration (sources footnoted on later pages). And, far too often, the need to use vials and disposable syringes has the unintentional effect of denying coverage and equity to hundreds of millions worldwide who require essential vaccines and medications, but who live too far from clinics, hospitals, or medical professionals.¹¹

* Medications have also been packaged in glass ampoules since the 1890s. This format creates major safety concerns since the glass must be broken to access the contents.



1850 Metal



1930 Glass



1980 Plastic

Additional limitations and problems include a long manufacturing lead-time for glass vials, glass flake contamination (see p. 12, item 7), vulnerability to breakage in transport, and wrongful reuse of disposable syringes among others.¹²

And, because too many clinics worldwide wrongfully reuse contaminated vials & syringes, diseases are unintentionally spread by healthcare providers.

This problem is officially unmeasured, but it is widely acknowledged by Gavi, WHO and other international and national health organizations. WHO statistics on this issue over the past 20 years have been sobering – and in some cases, frightening.

- Diseases spread by contaminated vials and syringes include an estimated 14% of all HIV cases worldwide.¹³
- Unsafe injections create an estimated 25% of all new Hepatitis B infections, harming 15 million patients per year.¹⁴
- For Hepatitis C, an estimated 8% of all new infections (1 million patients) result from unsafe injections.¹⁵
- An estimated 7% of all new bacterial infections result from unsafe injections (3 million cases a year).¹⁶

For non-healthcare professionals, it may be helpful to define these key terms:

- **“Coverage”** means providing populations with access to health services, affordably and of sufficient quality to be effective.¹⁹
- **“Equity”** is the absence of avoidable or remediable differences among groups of people whether those groups are economic, social, demographic or geographic. Inequity is a failure to avoid or overcome inequalities that infringe on fairness or human rights norms.²⁰

The problem is not confined to low-income countries. Dozens of U.S. outbreaks of Hepatitis were reported in the last decade.¹⁷ Experts believe many of these outbreaks were caused by clinical reuse of contaminated syringes.

In pandemics, contaminated vials and reused syringes can be disastrous. Injections from contaminated vials, caused by employing reused syringes and improperly sterilized needles, played a major role in some areas of the early Ebola outbreaks.¹⁸



To learn more about the issues with glass vials, read our booklet “Billions of Glass Vials Every Year with Unintended Consequences” or download it at bit.ly/apiject-red-booklets.

WHO's goals for health systems strengthening include safer, more cost-effective technologies.

The World Health Organization has long embraced a global agenda of “strengthening health systems” to deliver care “to those in greatest need, in a comprehensive way, and on an adequate scale.”¹³⁴

WHO's framework for action identifies six key building blocks for strengthening health systems. Among them: “A well-functioning health system ensures equitable access to essential medical products, vaccines and technologies of assured quality, safety, efficacy and cost-effectiveness, and their scientifically sound and cost-effective use.”¹³⁵ ApiJect is strongly aligned with these objectives. Its innovative design and materials enable safe, cost-effective delivery and use of vaccines and medicines. Quality is also assured because ApiJect works with UNICEF suppliers and with Contract Manufacturing Organizations that meet identical standards.

It's far too difficult to get fast, accurate data on population coverage of injectables.

Getting handwritten records back from the field, after healthcare workers have traveled from village to village giving injections to hundreds of remote populations, may be the best we have, but it is woefully inadequate.

As a result, global medical organizations do not have a reliable, real-time picture of how complete each injection campaign (or scheduled immunization program) has been, nor precisely where there are gaps in coverage. This lack of reliable feedback makes planning for future requirements extremely difficult to do well.

A truly modern reinvention of the total injection system can mitigate or eliminate all of these legacy drawbacks, saving millions of lives each year, while making billions of dollars of funding go farther each year to provide global coverage and equity.



The goal is global health coverage and equity of access

In places where coverage and equity are not achieved, the costs to the world's most vulnerable populations are high:

- Up to 1.9M of the world's children don't get routine vaccinations every year.²¹
- More than 3 million people die from vaccine-preventable diseases each year. About 1.5 million of these deaths are in children less than 5 years old.²²
- Every day approximately 830 women die from pregnancy- or childbirth-related complications, such as not having access to a trained professional who can inject a few cents' worth of Oxytocin or an equivalent.²³
- Gavi, the global vaccine alliance, estimates that worldwide, 300+ million children a year fail to get one or more needed injections.²⁴

SAFE MEDICAL INJECTIONS

10-Dose Glass Vials: The Old Solution is the New Problem

80% of all vaccines are distributed in multi-dose vials due to low purchase cost. But this works against full coverage, equity, waste control and safety.²⁵

The most popular format for delivering medicines and vaccines is often used in an unsafe manner that spreads death and disease. That format is the 10-dose glass vial, accounting for between 75% to 80% of global volume of injectable vaccines (90% in some areas).²⁶

The 10-dose vial saves money for healthcare providers because it comes with a lower upfront cost than a one-dose vial, the standard format used in most Western nations (although some vaccines come in multi-dose vials in the West, too). Not only does a 10-dose vial itself cost less per dose delivered, but the costs of filling, shipping, disposal, vaccine vial monitors and cold chain storage are also lower for 10-dose vials on a per-dose basis.²⁷

Yet despite its seeming efficiency, the 10-dose vial imposes substantial “hidden” costs.

• Hidden downstream costs:

A 10-dose vial may cost less for the purchaser, but these buyers don't see – or pay – higher downstream costs from what are often high levels of waste when unused vaccine or medicine is discarded.

• Missed opportunities to vaccinate:

WHO's 1993 global review found missed opportunities to vaccinate an estimated 30% of children and women. Reasons included health workers not opening multi-dose vials for a small number of persons to avoid vaccine wastage.²⁸ However, when workers decline to

vaccinate, in some countries as many as 32-46% of those turned away never return or receive vaccine.²⁹

• Contamination risk:

The incidence of injection-acquired diseases, as previously noted, indicates that despite the use of

preservatives in the contents of multi-dose vials, reused syringes too often contaminate those contents. All patients who subsequently receive injections from that vial have a risk of infection, even if clean needles are used. These drawbacks add up to a serious, even tragic, problem with 10-dose vials. The result: a format that is intended to save money (and extend supplies), actually costs untold lives per year. Its safety cannot be trusted.

Buyers typically focus on low per-dose catalog prices, but wastage (sometimes running from 20% to 50% or more) is routinely factored into bulk purchasing schedules.^{30,32} Yet, because the wastage is difficult or impossible to measure, the lower

price per dose purchased dominates. A format that is chosen because it seems to promise wider coverage, actually comes with perverse incentives to reduce or deny coverage in certain instances – such as when the (small) number of immediate patients at any given injection opportunity does not match the 10 available doses that fully utilize the vial's contents.



The 10-dose glass vial is the world multi-dose standard. And, that is the root of a big problem.



To learn more about iatrogenic infections from health clinics, read our booklet “When Injections Spread Disease” or download it at bit.ly/apiject-red-booklets.

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 ³¹

| 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 |

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

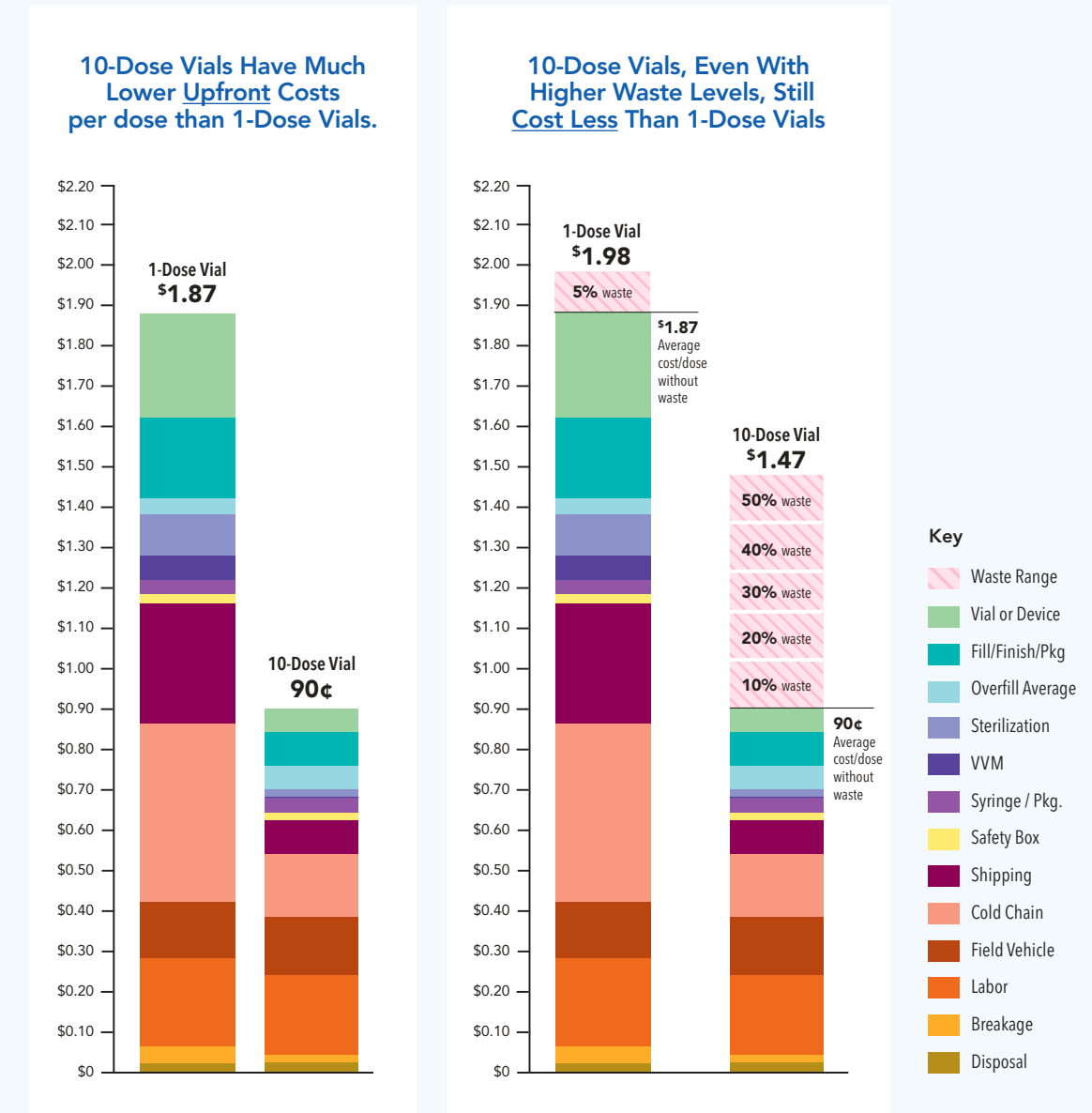
Health workers in many low-income countries wait until “enough” children are present to justify opening a vial, especially for lyophilized vaccines. (Liquid vaccines’ 28-day expiration can also result in double-digit wastage.)⁴³ Waiting to vaccinate several children at once results in many being turned away. Some patients never return to receive the vaccine, as shown in these studies from just two countries based on representative samples of health facilities.³²

Table 2 ³²

| | 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% |

Table 3 ³³

Comparing the Cost per Dose of 1-Dose vs 10-Dose Vials.



Figures shown do not include the cost of the injected vaccine. 25¢ per dose vaccine used to calculate overfill, waste, and breakage.

“Injection practices worldwide and especially in low- and middle-income countries (LMICs) include multiple, avoidable unsafe practices that ultimately lead to the large-scale transmission of bloodborne viruses among patients, health care providers and the community at large.”¹⁹⁷

— Dr. Margaret Chan
Former Director-General, WHO

THE APIJECT™ SOLUTION

SECTION 4

**Prefilled Syringes: The Safest Option.
Now They're Also the Lowest-Cost.**



ApiJect is a prefilled syringe that cannot be reused.

And, there is no glass vial to cross-contaminate.

Billions of Glass Vials Every Year, Each with Unintended Consequences and Problems

A 165-year-old technology won't get us to the level of coverage, equity and safety that the world needs today



1 Expensive to make, transport and use.³⁴
TCOD (Total Cost of Delivery) for each dose of vaccine or medicine can be as high as \$2.00 per injection. Manufacturing glass vials is expensive. Weight imposes higher transport costs.



2 Only medical professionals can give injections.
Vaccines and injections must be given by trained practitioners, but in much of the world trained medical staff are unavailable. Millions of patients don't get needed vaccines or medicines.



3 Easy to counterfeit.
Anyone can make or acquire glass vials and fill them with anything. This vulnerability contributes to a \$70-200 billion global counterfeit drug market, threatening the health of millions of patients.³⁵



4 Too easy to give patients the wrong medicine.
Since glass vials look virtually identical regardless of contents, it's easy for medical staff to mistake Drug A for Drug B, therefore patients can end up getting the wrong injection.



5 Too easy to give patient an inaccurate dose amount.
Healthcare professionals must withdraw precisely the right amount of vaccine or medicine from the vial. This requires knowledge and skill. It's easy to under-dose or over-dose a patient.



6 Contaminated vials and/or reusable syringes can be deadly.
UNICEF buys vaccines in AD syringes only. Other buyers may get disposable syringes that are wrongly reused, leading to 20 million+ high-risk infections per year.



7 Internal glass particles & flakes contaminate medicine.
Inside glass vials of vaccine and medicine, top layers of the glass surface can separate and flake off, usually at a scale invisible to the eye.³⁶



8 Glass vials and syringes break and are subject to costly recalls.
Vials and syringes break in the factory and during transport. In a 5-year period, glass breaking and flaking led to 100+ million vials or syringes being pulled off the market.³⁷



9 Short ID needles cannot be used with glass vials.
Longer needles are needed to withdraw liquid from vials. Injection then requires either a second, shorter needle or Mantoux style injections (often inaccurate for shallow intradermal injections, important for some vaccines).³⁸



10 Filling syringes uses nurses' and health providers' valuable time.
Particularly in busy clinics, time that could be spent treating more patients or spending longer with each patient, must instead be spent filling syringes.



11 Pollution from making 10 billion vials & 60 billion syringes yearly.
Manufacturing glass vials creates dust, waste and other pollution by-products. Producing a ton of glass from raw materials creates 384 pounds of mining waste.³⁹



12 High energy needs for glass are wasteful and costly.
Glass is one of the economy's most energy intensive industries. The total process uses high levels of natural gas and electricity (1% of total industrial energy use).⁴⁰



13 Manufacturing lead-time for glass creates slow crisis response.
Requirements for raw materials and glass manufacturing processes mean that vials must be ordered up to 6 months or more in advance. Too slow for rapid response during sudden outbreaks.⁴¹



14 Dangerous to discard due to needlesticks.
Disposal of used vials and syringes can be slow and even hazardous, exposing people to needlesticks, and creating possible exposure to leftover medication, etc. PATH reports 14% of cPAD users report fewer needlesticks; 36% said cPADs are easier to use.¹⁵⁹



15 Requires some patients to make ongoing clinical visits.
When only healthcare professions can give the injection, patient non-compliance increases because many find it difficult or impossible to visit clinics as needed.

THE APIJECT™ SOLUTION

The 30-Year Search for an Affordable 1-Dose Format

The global health community agrees that a low-cost mono-dose Auto-Disable device is needed. But, no affordable technology has appeared.

The global healthcare community understands that for many low- and middle-income nations, buying vaccines and medicines in 10-dose vials is a compromise – a difficult balancing act between cost, coverage, wastage and safety.

At the same time, public health officials have never given up hope that an affordable option would emerge that enabled every nation to make trustworthy mono-dose vials their standard choice of format.

In the quest for this improvement, health providers have turned to technology innovators to develop a new and safer alternative – the cPAD, or compact Prefilled Auto-Disable device – which they hoped could also be more affordable.

PATH develops the Uniject™ cPAD.

In the 1980s, the effort to develop a more affordable mono-dose injection format was launched by PATH, a nonprofit global health organization. With support from USAID, PATH developed an innovative, non-glass injection device called Uniject.™⁴²

Uniject™ does not have a traditional barrel syringe and plunger. It is a laminated, soft plastic container with a squeeze-bubble format. It is gamma-ray sterilized with an attached needle, then filled with medicine or vaccine in a separate step. The product is heat-sealed closed and foil packed ready for shipment.

Uniject™ offers several advantages over traditional syringes. The most important advantage is that its simple, squeeze-bubble delivery mechanism enables almost anyone, not just professionals, to administer injections easily and safely. And, it is a prefilled mono-dose device that can only be used once.



Developed at an R&D cost of more than \$50 million, Uniject™ was the first cPAD. Launched in the mid 1990s to widespread acclaim, the cost per dose was simply too high to scale.⁴⁵

Unfortunately, this did not happen for Uniject™. The cost of its multi-step, Form-Fill-Seal manufacturing process has remained high for nearly 30 years since its launch (see sidebar on facing page for details).

Uniject's cost: the key issue.

Uniject™ was a format breakthrough, because it offered greater safety at a price that was competitive with mono-dose vials. However, Uniject™ did not close the cost gap with 10-dose vials for per-dose delivery. (See Table 4 for details.)

Based on multiple studies, we estimate that Uniject's™ total cost is more per dose than a dose from a 10-dose vial, but less than a dose from a one-dose vial (see Table 4).

Sometimes, of course, a new technology is supported by the market in hope that its cost will come down as manufacturing efficiencies are found, economies of scale emerge, and rising demand enables manufacturers to earn revenues based on higher production volume.



Uniject's record in the field.

This cost differential between Uniject™ and 10-dose vials has worked against its universal adoption, even though Uniject™ has delivered 100+ million injections of contraceptive medicine and vaccines in low- and middle-income countries over the past decade or so.⁴⁶ While impressive, this represents a small percentage of the many billions of injections given worldwide each year.

PATH licensed Uniject™ to BD (Becton-Dickinson), the world's largest syringe manufacturer.⁴⁷ As part of the licensing agreement, BD supplies the Uniject system to pharmaceutical producers at preferential prices for use in low- and middle-income countries.

Gavi and WHO move to support AD syringes.

Since 1999, Gavi and WHO, along with UNICEF and UNFPA, the UN Family Planning Agency, have promoted non-reusable injection formats for ongoing programs and mass campaigns. UNICEF routinely buys vaccines in Auto-Disable syringes (although a significant number of other buyers still purchase vaccines in reusable syringes).⁴⁸ And, Gavi's 2000-2003 injection safety program helped 50+ countries switch to AD syringes.⁴⁴

Why Uniject™ is so costly to produce.⁴⁹

The Uniject™ cPAD is manufactured from multiple layers of plastic, using an 8-step "Form-Fill-Seal" thermoset lamination process. Individual steps often take place in multiple locations or facilities over the course of several weeks or months.

An overview of the Form-Fill-Seal process:⁵⁰

1. Resin layers are bonded into 5-layer sheets.
2. Sheets are transferred to another machine.
3. Sheets are run to form final shapes.
4. Two multilayer sheets are assembled around the Needle Hub to create a fillable form.
5. Bombard each empty form with gamma rays to sterilize.
6. Ship empty sterilized devices to a specialized filling system.
7. Strips are then loaded into another machine for automated 3-second fill of liquid.
8. Unit is quality-checked and closed through heat-sealing.
9. The device is labeled and foil wrapped.

THE APIJECT™ SOLUTION

Ready-to-Use Prefilled Syringes: The Fastest-Growing Injection Format in the U.S.

Designed for one-time use only, prefilled syringes are the safest choice because they can't become contaminated. They have traditionally been the most expensive format as well.

Prefilled syringes comprise an estimated \$5 billion global market, expected to reach \$7.5 billion by 2023.¹²³ This market mostly serves patients covered by insurance who self-administer medicines for chronic conditions such as allergies, diabetes or Hepatitis.

More than 100 drugs and vaccines are now shipped in prefilled syringes; and the number is steadily growing.¹²⁴ Suppliers include leading pharmaceutical manufacturers such as AbbVie; Bristol-Myers Squibb; Becton Dickinson; Eli Lilly; Amgen; Baxter; Bayer; Pfizer; F. Hoffman-La Roche; and Novartis.¹²⁵



Prefilled syringes are the preferred format in high-income countries for many reasons.

Fast Administration: Correctly filling standard syringes from a glass vial can be time-consuming. Taking time to accurately draw doses of medicine may delay treatment during medical emergencies such as drug overdoses and allergic reactions, where seconds count. Prefilled syringes save time; they can also save lives.¹²⁶

Dose accuracy: It is very easy to draw up an incorrect dose of medicine from a vial in a standard syringe.¹²⁷ With a prefilled syringe, the correct dose is ready to administer, which increases patient safety.

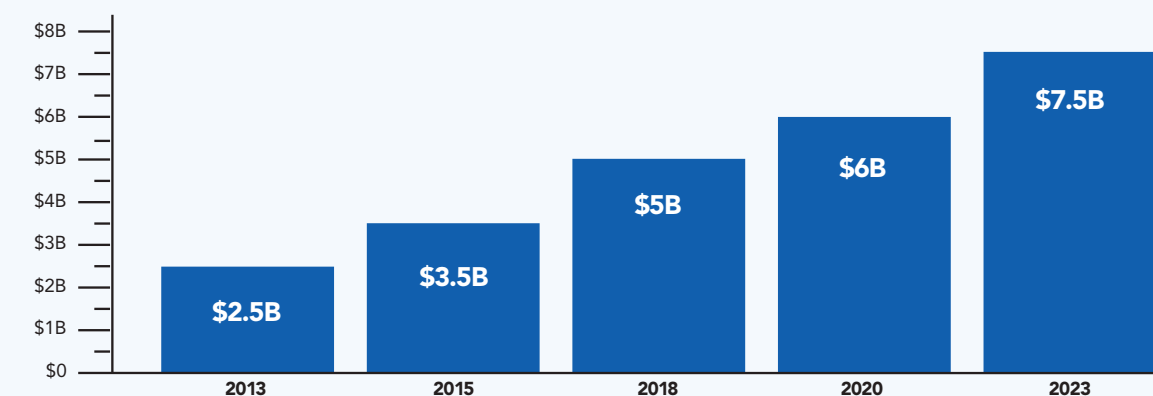
Shelf life: Most drugs and vaccines contain preservatives. Microbial contamination can still compromise sterility just hours after they are unsealed from a multi-dose glass vial. In properly stored prefilled syringes, medications can remain sterile and effective for 2-3 years.¹²⁸

Less waste: Glass vials and syringes are overfilled by 20-30% to compensate for waste (including difficulty retrieving the vaccine or medicine). Prefilled syringes require less than 2% overfills, enabling the same amount of vaccine or medication to provide 18-23% more doses.¹²⁹

Improved safety: Prefilled syringes are disposable, single-use devices. They cannot transfer diseased blood from the first patient to the second patient. There is no glass vial to become contaminated, either. Result: patients can trust that the prefilled format is safe.

Convenience and Self-Treatment: Taken together, these advantages make prefilled syringes a safer choice than medication administered with standard syringes and glass vials. Prefilled syringes are more suitable for community health workers and for self-administration, which is why these applications have been approved already on a limited basis for certain drugs. If regulators permit, expanding the base of health workers who can give injections could greatly increase coverage and adherence, especially in low-resource settings.

Global Prefilled Syringes Market Growth
Dollar Volume in \$ Billions



Prefilled syringes also have numerous drawbacks and challenges.

Cost has been the most significant drawback of prefilled syringes. Compared to a traditional single-dose glass vial and syringe that costs about \$1.00, a prefilled syringe may cost \$5.00 to \$10.00 per unit for some applications (such as common self-administered medicines) or even \$20.00 to \$30.00 per unit for advanced applications such as surgical anesthetics.¹³⁰

A second problem with prefilled syringes is the complex manufacturing processes that are required. Older production techniques sometimes allowed air bubbles to get into the syringe chamber during the filling phase. New methods for in-line vacuum filling and inserting rubber stoppers, eliminate bubbles but cost more.

Another manufacturing challenge for prefilled syringes is sterilization. This critical step must be performed either by gamma radiation or by autoclaving, which is a high-temperature pressure chamber process that creates a pH shift in glass syringes. (Glass is still used for more than half of all prefilled syringes.¹³¹)

The need for separate steps to sterilize all components of a prefilled syringe prior to filling, and then the follow-up procedures for filling and handling to preserve sterility, add complexity and cost.

The ideal solution would be a low-cost prefilled syringe that could be manufactured and sterilized with simpler technology.

If prefilled syringes cost the same as traditional syringes and glass vials, they would become the world's preferred injection format because of their many advantages.

To strengthen health systems worldwide, and to better serve the world's seven billion patients, a low-cost prefilled syringe is needed that can be produced at scale with fast, simple and reliable manufacturing technology, to provide a trustworthy alternative.

 To learn more about the benefits of a low-cost single-dose injection, read our booklet "How a Low-Cost Mono-Dose Syringe Can Increase Safety" or download it at bit.ly/apiject-red-booklets.

Table 4 ⁵¹

Comparing the Total Cost per Dose of Vaccine Delivery

Costs shown do not include cost of vaccine injected

Scenario: **Drug is 25¢ per dose** (used for calculating overfill, breakage, waste)

| Purchase Cost (Upfront) | ApiJect | 10-Dose Vial per dose | Uniject™ | 1-Dose Vial |
|-------------------------------------|----------------------------|-----------------------|------------------------|------------------------|
| 1 Vial (or cPAD) | \$0.04 | \$0.065 | \$0.25 | \$0.25 |
| 2 Fill/Finish/Pkg/Overhead | \$0.01 | \$0.09 | \$0.30 | \$0.20 |
| 3 Overfill | \$0.01 | \$0.05 | \$0.01 | \$0.05 |
| 4 Sterilization | \$0.01 | \$0.02 | \$0.05 | \$0.10 |
| 5 VVM* | \$0.05 | \$0.005 | \$0.05 | \$0.05 |
| 6 UNICEF vaccine purchase price | \$0.12 diff. +/- | \$0.23 +91% | \$0.66 +464% | \$0.65 +453% |
| 7 Syringe/Needle Hub (ex. shipping) | \$0.20 | \$0.04 | \$0.00 | \$0.04 |
| 8 Safety Box | \$0.01 | \$0.02 | \$0.01 | \$0.02 |
| 9 Shipping (Air/Truck) | \$0.04 | \$0.08 | \$0.04 | \$0.30 |
| 10 Purchase Cost per Dose | \$0.37 diff. +/- | \$0.37 0% | \$0.71 +94% | \$1.01 +175% |
| Field Costs (In Country) | | | | |
| 11 Cold Chain + All Storage | \$0.20 | \$0.16 | \$0.57 | \$0.45 |
| 12 Field Vehicle + Transit Labor | \$0.14 | \$0.14 | \$0.14 | \$0.14 |
| 13 HCW Labor | \$0.10 | \$0.20 | \$0.10 | \$0.22 |
| 14 Breakage | \$0.00 | \$0.01 | \$0.00 | \$0.03 |
| 15 Disposal | \$0.01 | \$0.02 | \$0.01 | \$0.02 |
| 16 Field Cost per Dose | \$0.45 diff. +/- | \$0.53 +18% | \$0.82 +82% | \$0.86 +91% |
| 17 Total Cost/Dose Pre-Waste | \$0.82 diff. +/- | \$0.90 +10% | \$1.53 +87% | \$1.87 +129% |

Wastage plays a large role in the total cost of vaccines delivered in Low- and Middle-Income Countries. Wastage rates for multi-dose vials are significantly higher than single-dose formats. We took a reasonable average of 25% wastage for multi-dose and 5% for single-dose.

| | | | | |
|--|----------------------------|-----------------------|-----------------------|------------------------|
| 18 Waste % | 5% | 25% | 5% | 5% |
| 19 Waste Cost | \$0.05 | \$0.29 | \$0.09 | \$0.11 |
| 20 Total Cost of Delivery (excludes cost of vaccine) | \$0.87 diff. +/- | \$1.18 +36% | \$1.62 +86% | \$1.98 +127% |

* Only required for drugs in the Cold Chain.



To learn more about ApiJect's costs, read our booklet "Comparative Analysis of Total Injection Cost" or download it at bit.ly/apiject-red-booklets.

THE APIJECT™ SOLUTION

ApiJect is a Delivery Device (BFS + Needle Hub) Designed to be the Lowest-Cost, Safest Option

Prefilled single-use "soft" syringes made with proven BFS technology can help the world achieve 100% coverage, access and safety.

A low-cost, integrated injection solution can strengthen health systems worldwide.

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 unit-dose system that costs *less per dose upfront* and also costs *up to 50% less per dose delivered depending on wastage costs*.⁵²

ApiJect's cost advantage enables any country to stretch its health budget farther and move closer to full coverage and equity while eliminating contamination.

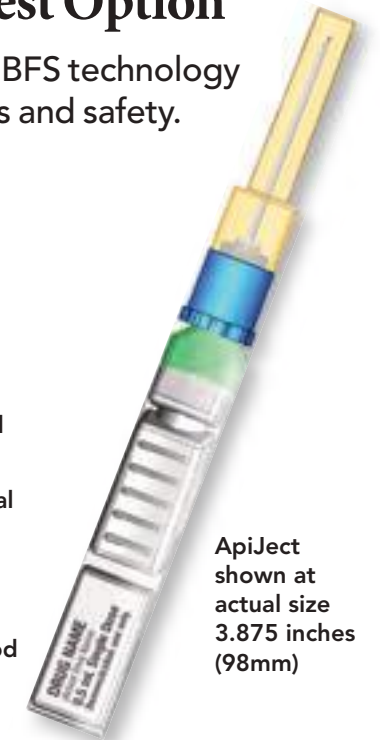
In Phase 2, this same prefilled single-use syringe will, just by touching a mobile phone, provide built-in, real time, healthcare data communication that enables healthcare providers to track coverage rates and GPS locations, then use this information to better target their budgets, personnel and planning strategies.

The first next-generation cPAD.

The ApiJect device is comprised of three components. First, a squeezable plastic container that contains a precise sterile prefilled dosage of a vaccine or medicine. Second, a connector mount; and third, a sterile hub that disables the device after one use and includes a double-ended needle of the desired gauge and length for that medicine or vaccine, with a safety cap.

ApiJect essentially replaces the traditional glass vial with the squeezable plastic container, while also replacing the disposable syringe with an appropriate-sized attached

- Single-Use
- Small
- Lightweight
- Unbreakable
- Prefilled
- Precise Dose
- Color/Shape Coded
- Inexpensive
- Includes Vaccine Vial Monitor
- 3 Needle Sizes
- Hard to Counterfeit
- Short training period
- Pre-assembled or User-assembled



ApiJect shown at actual size 3.875 inches (98mm)

needle and its safety cap. As a result, there is no need to use the syringe's needle to withdraw a precise quantity of vaccine or medication from a small glass vial to load the syringe – and no risk of vial contamination. Instead, the correct dose is prefilled so no dosing or calibration is required from whoever gives the injection; a needle of the right gauge and length is attached for each injection. This duplicates the benefits of today's far more expensive prefilled syringes or even BD's Uniject™.

As with Uniject™, to activate an ApiJect the user simply pushes the Needle Hub and the "liquid container" together. ApiJect delivers the correct dose when the administrator (nurse, CHW, medic, etc.) squeezes the top chamber, with very little force. As with a cPAD, the entire ApiJect process is easy, intuitive and non-threatening.

ApiJect: a multi-component system.

Again, ApiJect is a multi-component system for a prefilled syringe made of soft, medical-grade plastic. There is no barrel or plunger. Instead, the administrator simply inserts the needle in the patient and then squeezes the first chamber in a two-chamber configuration. The air in the first chamber then pushes the liquid medicine or vaccine in the second chamber through the needle and into the patient.

The Technology: Blow-Fill-Seal (BFS).

Each part of the ApiJect System is manufactured at very high speeds in a sterile form using a well-established manufacturing technology called Blow-Fill-Seal (BFS).⁵³ Both the plastic container and its content (i.e., vaccines) are automatically machine-integrated during a high-speed sterile manufacturing process.

BFS is a trusted, widely used technology for packing pharmaceutical grade liquids, delivering 50 billion doses of sterile eyedrops and eardrops annually, along with a smaller number of parenteral applications. It is also being used for an oral rotavirus vaccine from GSK.¹⁶²

ApiJect utilizes reliable BFS technology with an attachable Needle Hub to bring BFS' natural advantages of cost, speed and ease of use to the world of injections. BFS is the ideal choice to meet the modern world's high-volume demand with the ability to produce up to 30,000 finished devices per hour, per machine, with no extra steps.⁵⁴ BFS' end-to-end manufacturing process allows for the highest possible speed and scale.

Strengthening health systems in critical ways.

ApiJect brings more than a dozen valuable advantages to everyone who uses healthcare today and to more than a billion people who are not being well served by the

current injection system of glass vials and traditional syringes. Six of the most important benefits include:

1. At last, a prefilled, single-dose delivery system that has a lower total cost per dose than the per-dose cost of a 10-dose vial.

ApiJect reduces TCOD (Total Cost of Delivery) of each dose of vaccine or medicine to a patient by an average 20-50% from the lowest cost alternative, often more.

With ApiJect, a single dose of a vaccine or medication can be delivered for 87¢ per injection.⁵⁵ By comparison, 10-dose injections cost, on average, about \$1.18 to \$1.98 per dose delivered when waste costs are added to raw materials, manufacturing, packing, shipping, cold chain, administration and disposal.⁵⁶ See Table 5.

2. One-time sterile injection prevents the spread of infection.

Like auto-disabled or safety syringes, ApiJect prevents reuse and contamination, bringing all buyers into compliance with WHO standards.

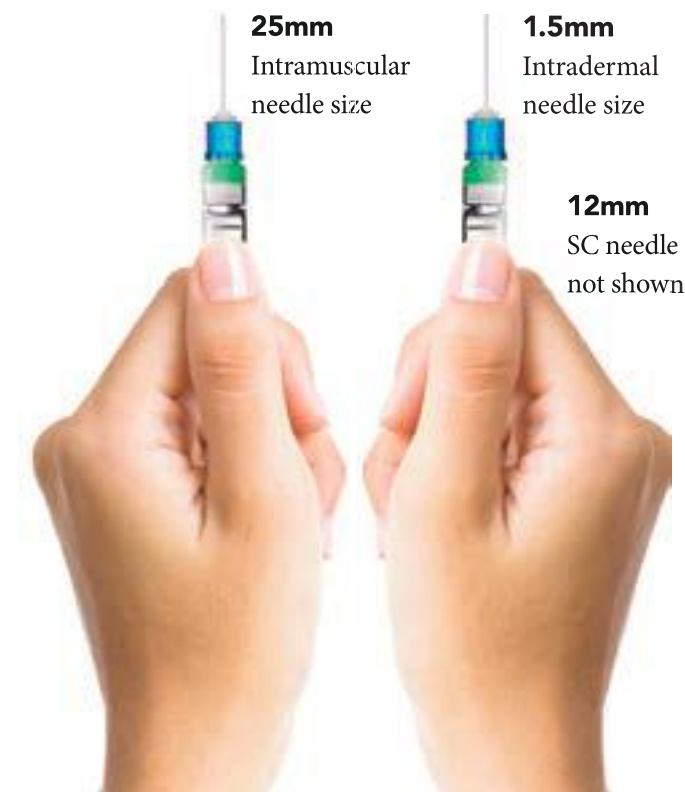
The medicine is filled aseptically in the BFS container, which is then sealed. The Needle Hub is also sterilized in production; a separate seal is attached to keep the hub sterile until activation. In addition, ApiJect cannot be reused or refilled, ensuring no danger of vial or needle contamination.

3. When permitted by authorities, many more community health workers will be able to give injections with minimal training.

ApiJect means that health ministries and agencies will have the option, at their discretion, of permitting injections of all kinds to be given by up to 2 million or more community health workers (CHWs) worldwide – including midwives who are not licensed practitioners.⁵⁷

If health agencies decided to permit all CHWs to give injections, this would have a significant impact on global health. Currently one in five children worldwide (400 million people) are “untouched by vaccines,” said WHO's vaccine director.⁵⁸ In the developing world, millions of mothers give birth unattended by medical staff; and thus they and their newborns cannot get timely injections of vaccines such as those for tetanus or Hepatitis B.⁵⁹

According to Dr. Henry Perry, senior scientist at the Johns Hopkins Bloomberg School of Public Health, “If CHWs are used to deliver the interventions they are capable of delivering and if 100% coverage could be attained, then the lives of 3.6 million children would be saved every year.”⁶⁰



4. Shallow injections of vaccines no longer require special injection skill.

Many vaccines and medicines require an intradermal (ID) injection, which uses a significantly smaller needle than a standard intramuscular (IM) injection. But since the longer IM needle is needed to pierce the rubber stopper and withdraw the medicine from the vial, the healthcare worker is forced to do a far more difficult shallow injection, using the Mantoux-style. ApiJect can be affixed with a subcutaneous (SC) or ID needle, allowing for a standard injection procedure that is significantly easier and far less painful than the Mantoux-style.

5. When appropriate and approved, family members or patients can self-administer.

ApiJect reaches the places and people that can't be reached by glass vials today. In low- and middle-income nations, especially in places lacking medical staff, the option of safe, easy self-injection is a world-changer. For example, women or family members can self-administer contraceptives on a quarterly schedule. And, for patients with chronic conditions that require injections over time, self-injection using ApiJect can meet this need long after healthcare workers have left an area. In the West, the option of self-administered one-time injection can increase the number of patients who will remain current on longer-term courses of treatment.

6. A two-second test eliminates counterfeits.

Pharmaceuticals are the world's biggest counterfeit market (\$200 billion for pills, syrups and injectables).⁶⁴ Phony drugs endanger millions of patients. ApiJect is extremely difficult to counterfeit. It embeds highly visible official logos within the walls of the plastic chamber (not touching the drug). These embedded logos cannot be scratched off genuine products. Users of ApiJect can instantly verify legitimacy, eliminating the danger of using counterfeits.

ApiJect Offers Many Additional Benefits:

- **Improved dose accuracy.**

Chances of injecting incorrect drugs are reduced because ApiJect containers not only come in different colors, and different shapes – unlike glass vials, but also will have the name of the drug and the dosage clearly marked on the label. And, since every dose is prefilled, the device eliminates dosing errors from drawing up the wrong dose from a glass vial.

- **Surge capacity due to much faster production.**⁶⁵

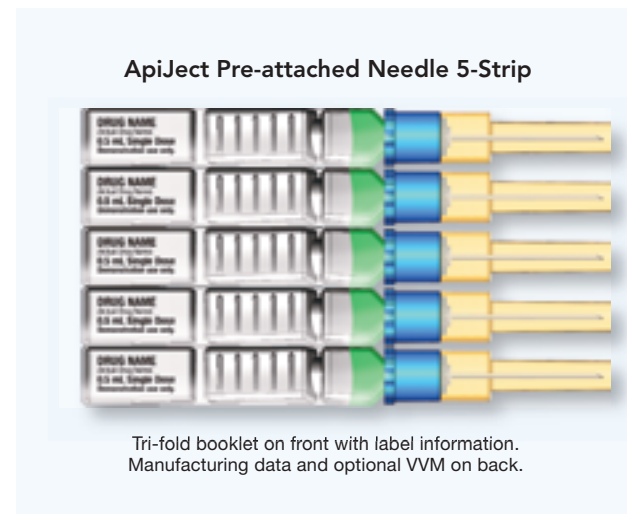
Raw materials requirements and manufacturing processes mean that glass vials must be ordered 6 months or more in advance – which can be far too slow for a rapid response when more drug or vaccine is quickly needed during an emergency outbreak.⁶⁶ ApiJect can be manufactured in as little as a couple of hours once the bulk medicine or vaccine arrives, making it more suitable for rapid campaign response in case of outbreaks or emergencies.

- **Convenient, faster, and reduced human error.**

Traditional glass vials and syringes can require 10-12 steps to prepare and administer each injection (the most critical and time-consuming of which is accurately filling the syringe from the vial).⁶⁷ Using ApiJect requires just five steps. After hand-washing, providers: 1. press the Needle Hub and container together until a "click" is felt to activate the syringe; 2. uncap the needle; 3. clean the injection site; 4. give the injection; and 5. safely dispose of the device.

- **Improved patient adherence with regimens.**

When only professionals can give injections, many patients who need recurring injections often stop getting them. They may find it difficult to visit clinics, or they may



dislike repeat visits and the associated costs or disruptions.

With the option of self-injection at home (when deemed appropriate), ApiJect makes it much more convenient and appealing for patients to continue with long-term treatment regimens. Family administration or self injection are potential game-changers for MDR-TB and other long-term chronic disease therapies.

- **Safer to discard.**

Disposal of used vials and syringes can be hazardous due to needlesticks, cuts from broken glass vials, exposure to leftover medication, etc. ApiJect's lack of glass, plus its needle safety cap and smaller size (easier to manipulate) reduce these hazards, making disposal safer.¹⁶⁰

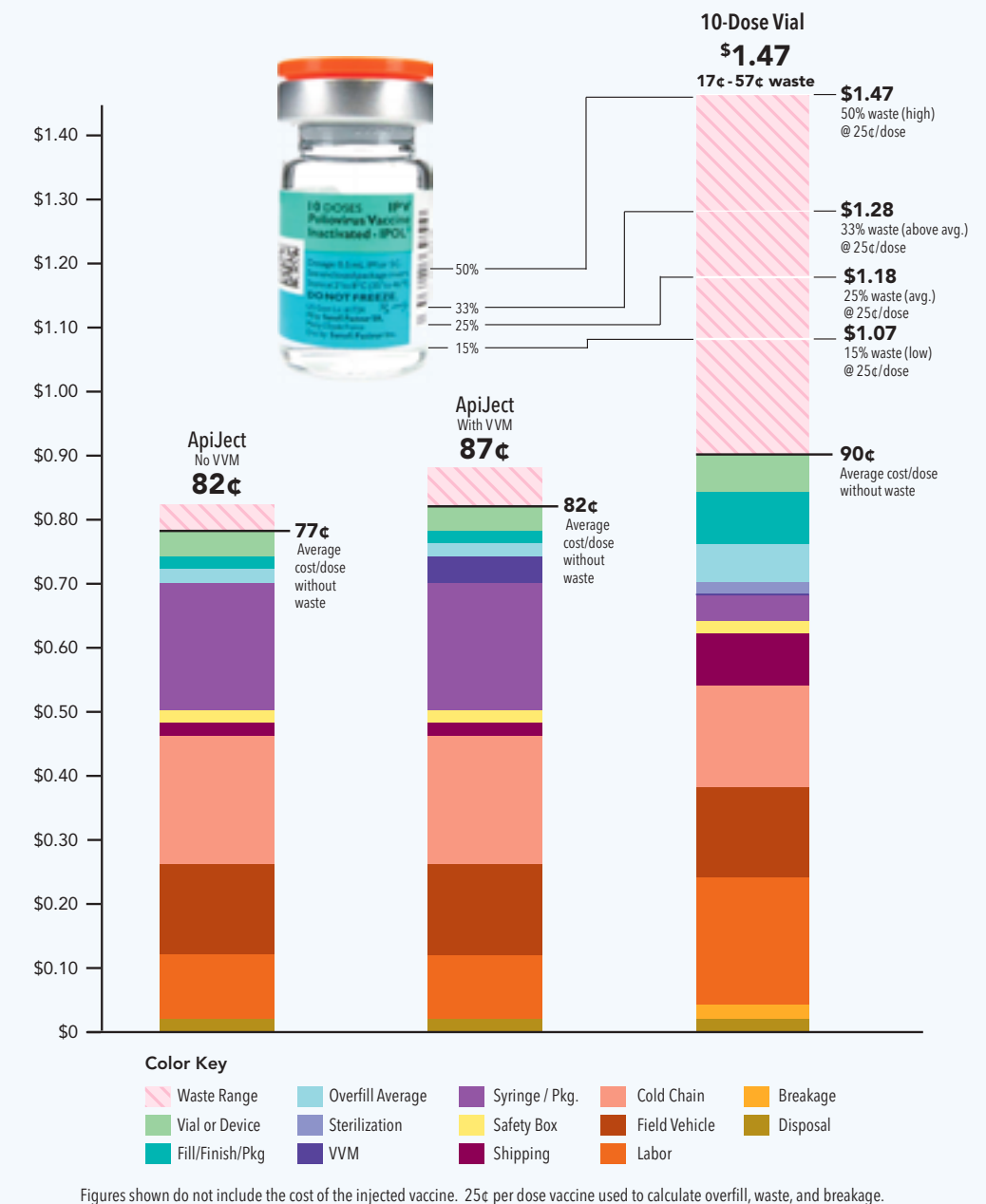
- **Significantly less adverse environmental impact for both energy and waste.**

Compared to energy-intensive glass manufacturing, ApiJect's small-footprint plastics manufacturing process uses 80% less raw materials and thereby consumes 75% less energy, generating 80% less pollution and 15% less waste product.⁶⁸ Less material usage requirements leads to less pollution, regardless of disposal method.

Table 5⁶⁹

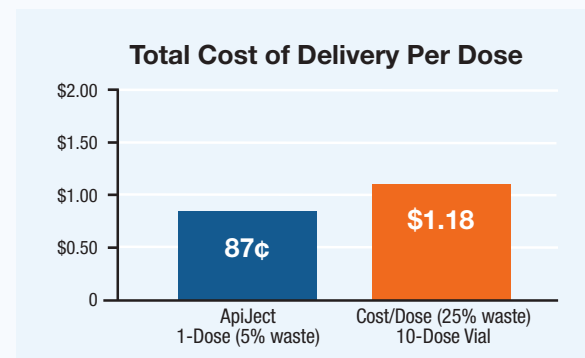
ApiJect Costs Far Less per Dose than 10-Dose Vials. The Higher the Actual Waste, the More the Savings.

20-50% savings per dose is typical. 60% or more is achievable.



The ApiJect™ System Costs 20-50% Less per Dose than 10-Dose Vials

And, it delivers critical global health benefits such as coverage, equity and safety at no additional cost



1 Typical cost savings 20% - 50% less than a 10-dose vial.⁷⁰

Reduces TCOD (Total Cost of Delivery) of each dose of vaccine or medicine to a patient by 20% to 50%. Using glass vials and syringes to deliver a 25¢ vaccine costs an average of \$1.07 - \$1.47 per injection in 10-dose form not including the cost of the injected vaccine. ApiJect costs an average of 87¢ per dose delivered.



2 Millions of community health workers can now give injections.

Where permitted, vaccines and injections can now be safely given by additional unlicensed practitioners, including midwives, where medical staff are unavailable. This new option can bring vaccines and medicines to the 20% of people worldwide who don't regularly get them now.⁷¹ Supports Gavi and WHO goals for global coverage and equity.



3 Health agencies can permit patients to self-inject safely.

In some nations, remote areas often lack medical staff. If authorities approve, a birth attendant can inject a mother with Oxytocin after childbirth; others can self-inject various vaccines or medicines. In the West, self-injection will likely increase patient adherence to long-term treatment regimens.



4 Shallow injections (intradermal) no longer require special skill.

Longer needles are needed to withdraw liquid from vials, but they require Mantoux-style injections (often inaccurate for shallow intradermal injections, important for some vaccines.⁷² ApiJect is prefilled, designed and configured so it can utilize the very short needles required. The result? ID injections are easy and more effective.



5 Virtually eliminates counterfeit drug injections.

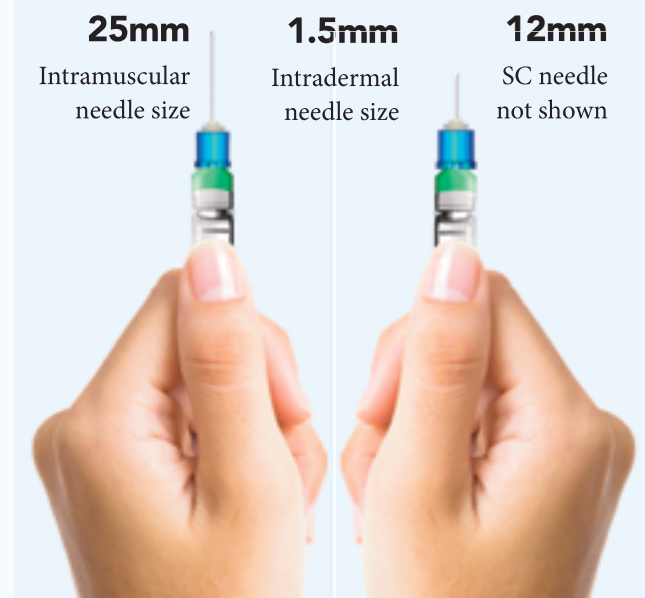
ApiJect embosses official logos into the plastic container that can't be scratched off or tampered with. Users can instantly verify genuine products, virtually eliminating injectables from the staggering \$200 billion a year in counterfeit drug sales that plague much of the world.⁷³



6 Right drug, right dose, right needle – made simple.

There's less risk of mistaking Drug A for Drug B because ApiJect can come in clearly-labeled containers of different shapes and colors. Prefilled volumes eliminate dosing errors. And, only the right size needle for each injectable is supplied with the container.

- 7 Single use only.**
No reuse prevents spread of disease.
- 8 Rapid training.**
Virtually any adult or teen can use.
- 9 85% less energy used.⁷⁵**
Manufacture, transport & storage savings.
- 10 75% less waste from mfg.⁷⁶**
No by-products, no glass landfill, etc.
- 11 Safer to discard.**
No broken glass.
- 12 Saves nurses & doctors time.**
No need to carefully fill syringes.



THE APIJECT™ SOLUTION

BFS – A Proven Packaging Technology With 50+ Years of Experience and Reliability

Blow-Fill-Seal manufacturing has been used billions of times for sterile respiratory and ophthalmic products since the 1960s. Now it is ready for injectables.

It may seem surprising that after decades of searching for a technology for an affordable mono-dose injection format, a solution has finally emerged. Perhaps even more surprising is that this technology has been used by segments of the global health market for decades.

The technology used by ApiJect to achieve a cost/quality breakthrough for injection devices has been in continual use since the 1960s. It's called Blow-Fill-Seal manufacturing (often referred to as "BFS") and is in use worldwide.⁷⁷

BFS is a high-efficiency, low-heat, low-cost manufacturing method used to produce a wide range of liquid-filled containers. A single machine forms, fills and seals the container. First, plastic resin is melted by an extruder at high temperature and pressure, forming a molten plastic tube. The tube is filled with liquid medication and sealed. The entire process takes 3 to 15 seconds.

BFS today is well established as a highly affordable and reliable choice for sterile delivery of over the counter treatments and prescription drugs. These include respiratory and ophthalmic products, certain medicines taken by mouth and some parenterals (IV solutions).

Billions of doses of medicine have been safely delivered to patients worldwide using BFS containers starting in the 1960s. The pioneering inventor of BFS is Rommelag, a family-owned company based in Sulzbach-Laufen, Germany that remains the worldwide industry leader.⁷⁸ In a visionary insight, Rommelag realized some years ago that prefilled mono-dose "blisters" created using BFS technology could be combined in-line with the proper hypodermic needle to allow for the easy injection of the fluid within the blister. A key advantage would be a much lower cost than existing injection formats for both vaccines and medicines – specifically glass vials and standard syringes.

Rommelag experimented with a variety of methods to accomplish this while steadily investing in improved engineering for their machines, which the company sells worldwide to a wide range of industries. Despite considerable efforts, company engineers did not develop a solution that they deemed ready for market.

A critical insight required to bring Rommelag's vision to reality was provided by Marc Koska, inventor of the K-1 Auto-Disable Syringe. Mr. Koska had been seeking a new way to create an affordable, prefilled mono-dose AD syringe format. He was inspired in part by Uniject™, the first cPAD, a high-cost Form-Fill-Seal AD mini-syringe with an integrated needle element. He knew that a more

affordable process was necessary – and he realized BFS could be the answer. But how would the needle work?

Mr. Koska's key insight: rather than attaching a needle as part of the initial BFS manufacturing process, there could be a separate, pre-assembled hub that housed a double-ended needle. This hub would then be plugged into a connector mount on the BFS container as a post-filling finishing step.

He proceeded to design ApiJect, a BFS cPAD device that used BFS containers and an attachable needle housing hub. ApiJect promises to unlock the power and benefits of BFS as a competitor to the current standard of 10-dose vials with syringes that withdraw and then inject vaccines.

Mr. Koska knew that BFS manufacturing offers a large cost advantage over glass manufacturing of vials and plastic manufacturing of traditional barrel-and-plunger type syringes. It is also much more affordable than the multi-step laminate process used for Uniject™.

Beyond cost, Mr. Koska discovered that there are a number of additional factors that make BFS a truly superior alternative to traditional multi-dose vials. Among them:

1. Rapid, high-volume manufacturing
2. Consistent dose accuracy
3. Minimal to no training required
4. In-line sterilization
5. Faster administration
6. Reduction in human errors
7. Small footprint for BFS machine
8. Infinite customization potential

Rommelag's BFS is the right technology at the right time, and ApiJect is the right invention to bring affordable mono-dose vaccines and medicines to the world.

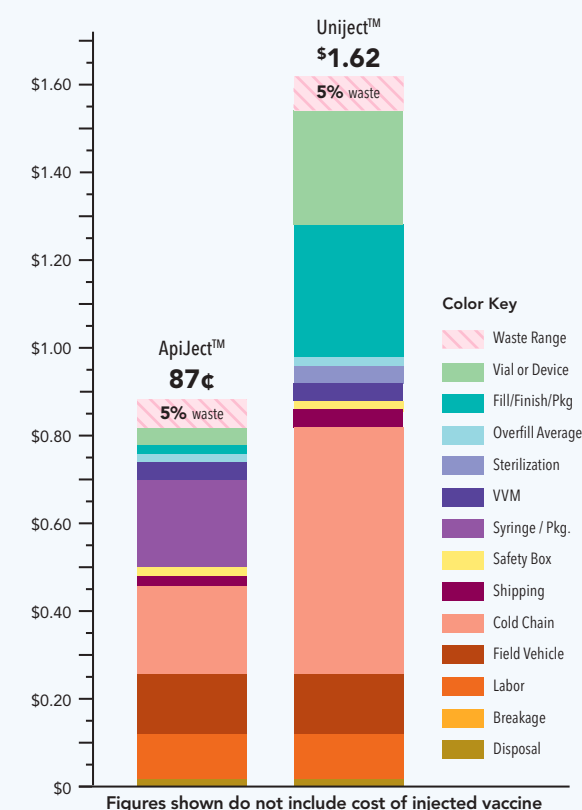
To learn more about how ApiJect's manufacturing, read our booklet "How We Manufacture a Prefilled Syringe" or download it at bit.ly/apiject-red-booklets.



Rommelag state-of-the-art contract BFS production facility in Zell, Switzerland supports Bio-safety Level 2 processes.

Table 6⁷⁹

BFS Delivers Dramatic Cost Savings



THE APIJECT™ SOLUTION

BFS Enjoys Broad Regulatory and Consumer Acceptance

The FDA and CE have long recognized BFS as an effective aseptic technology. Each year, BFS containers supply more than 50 billion doses worldwide.

The advantages of Blow-Fill-Seal (BFS) technology for pharmaceuticals and medicines have been hiding in plain sight for decades – especially in the U.S. As recently as 2010, few U.S.-based pharmaceutical manufacturing executives had personally seen a BFS manufacturing installation.¹⁰⁵ This might be considered somewhat surprising, given the fact that by then BFS containers had been used for decades to deliver high volumes of sterile products both in the U.S., Europe, and Australia.

According to the FDA, most U.S. medicinal applications of BFS have been, and remain, ophthalmics and respiratory care products.¹⁰⁶ The situation is different in Europe, where certain classes of injectables are widely supplied in BFS containers as well.¹⁰⁷ For example, Europe's largest IV facility employs BFS technology.¹⁰⁸



PATH, world's leading medical technology NGO, worked with Rommelag, the pioneering BFS inventor and manufacturer, to produce this MMD (multi mono-dose) BFS oral form factor.

Acknowledged by the FDA

The FDA has acknowledged since 2004 that BFS confers definite advantages for medicinal delivery. The FDA's 2004 publication, "Guidance for Industry – Sterile Drug Products Produced by Aseptic Processing," remains its current statement on BFS standards. That document notes:

"[BFS] is an automated process by which reservoirs are formed, filled, and sealed in a continuous operation. This manufacturing technology includes economies in reservoir closure processing and [also in] reduced human intervention... Advantages of BFS processing are known to include rapid reservoir closure processing and minimized aseptic interventions."¹⁰⁹

Superior sterility

Driven by growing regulatory acceptance, and based on improving manufacturing processes and products, BFS for pharmaceutical liquids have grown steadily during the past 20 years. Manufacturers have engineered a series of enhancements that increase product integrity and help guarantee patient safety.¹¹⁰ One example: New methods have been developed to keep air from the surrounding environment out of the containers during filling, using positive airflow technology.¹¹¹ Any particulates created from cutting and sealing the plastic container are pushed outward; there's no inflow from the outside environment. Environmental monitoring verifies the lack of non-viable particles in the final product.¹¹²

Manufacturers have also developed advanced ultrasonic techniques for sterile finishing while machines slice the top of a formed Blow-Fill-Seal container.¹¹³ As a result,

BFS has demonstrated that it can achieve what has been termed a "drastic reduction" in foreign particulates compared to the reported industry average.¹¹⁴

Challenge studies on aseptic BFS systems started in 1990 through 2011 and beyond. They demonstrated the ability for BFS manufacturing processes to produce vials "free" of viable microorganisms, with endotoxin levels in the acceptable range, while producing high sterility assurance levels (10⁻⁶ SAL) throughout the manufacturing process.¹¹⁵

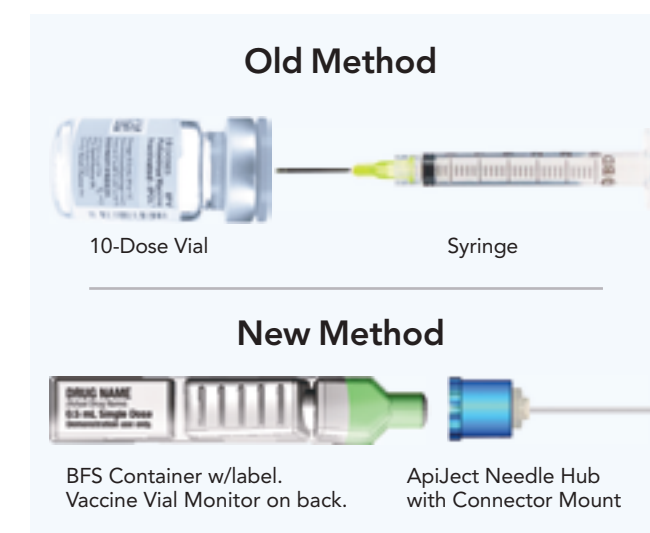
Innovations for temperature control

A critical issue for vaccines, biologics, proteins, and other complex solutions is their vulnerability to degradation in quality and effectiveness due to any long-term exposure to elevated temperatures. For many vaccines, conventional sterilization cannot be employed.¹¹⁶

BFS avoids this problem. Heat sensitivities of contents do not lead to degradation of quality for medicines and vaccines when they are handled with the most recent BFS technology. BFS engineers have developed methods to keep containers cooler during the manufacturing, filling and sealing process, which takes just 10 -15 seconds from start to finish.¹¹⁷ The rapidity of the process also serves to minimize or eliminate any temperature effects on vaccines.



BFS offers almost unlimited flexibility in container shape and size – but has never had an attached needle for injections.



Little chance of drug-container interaction

One key consideration for BFS technologies is the question of whether any of the plastics used to manufacture the containers could interact in a negative way with the vaccines or medicines that fill them. For example, no "leaching" must occur (plastic molecules dissolving into medicine).

BFS manufacturing predominantly employs two resins: polyethylene and polypropylene. The FDA generally views these substances as inert. They contain no additives. Their permeability by water vapor is minimal. In addition, containers made of these plastics may be handled safely and easily in critical care sites, including clinics and hospitals. International regulators have broadly classified BFS resins as acceptable for pharmaceutical liquids.¹¹⁸

Pharmaceutical manufacturers, regulatory bodies, global health organizations and other key players increasingly recognize that BFS offers a viable solution to many challenges that stand between them and global healthcare coverage and equity.

To learn more about the potential impact of a single-dose format like ApiJect, read our booklet "How Low-Cost Mono-Dose Syringes Enable Many Use Cases" or download it at bit.ly/apiject-red-booklets.

A single unit of the latest Blow-Fill-Seal manufacturing machine can produce more than 200 million sterile, aseptically prefilled ApiJect devices per year.

OVERVIEW

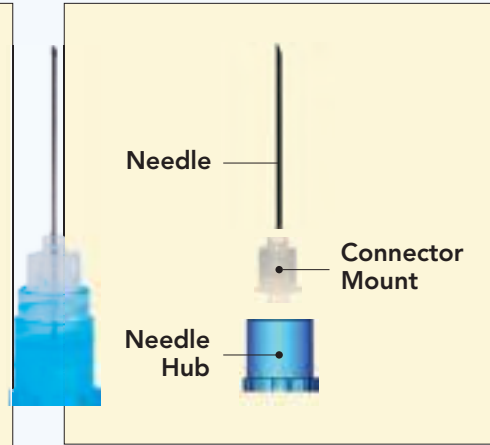
A BFS machine aseptically forms 20-25 drug containers, aseptically fills them with medicine and then cools, seals and inspect each one.

A 2nd machine trims and cuts; a 3rd machine affixes sterile connector mounts and ApiJect Needle Hubs.

The entire process takes 10-15 seconds, start to finish. Specifics follow.

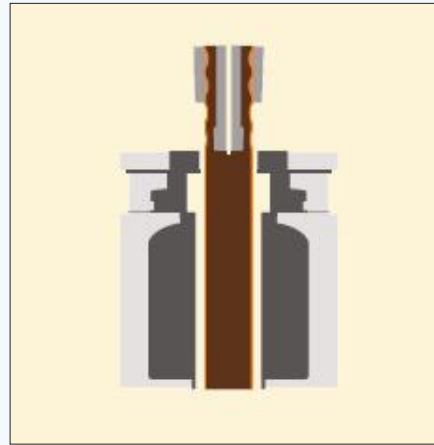


In just 5 minutes, prefilled ApiJect System syringes containing 2,000 individual doses are aseptically manufactured in a continuous belt, auto-fed into a cutter. End result: single syringes or strips of 5, 10 or more.



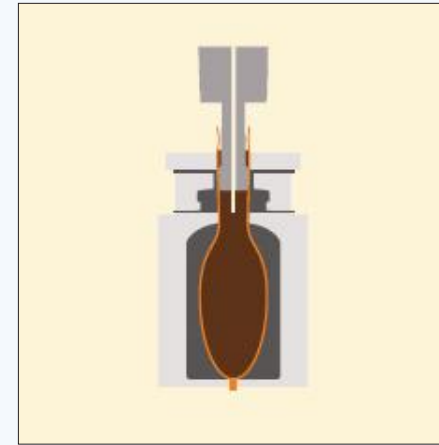
1 Prefabrication and Sterilizing

At a separate location, connector mounts and Needle Hubs are prefabricated and sealed, then sterilized with Ethylene Oxide (gas under vacuum).



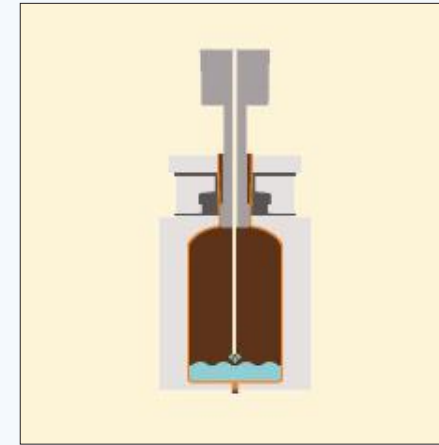
2 Aseptic Extruding

At a BFS site, soft, heated polymer is extruded (pushed out) of manufacturing machine as "parisons" (open tubes) into machine's Class A clean space (no sterilization needed).



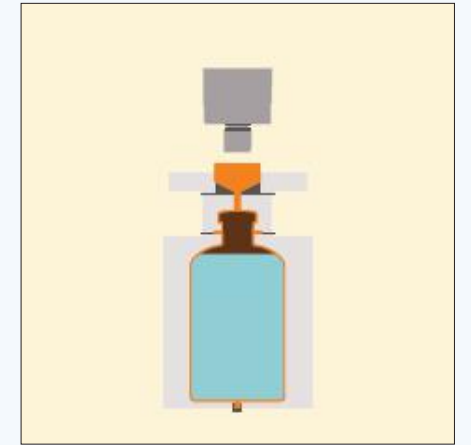
3 Aseptic Blowing

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.



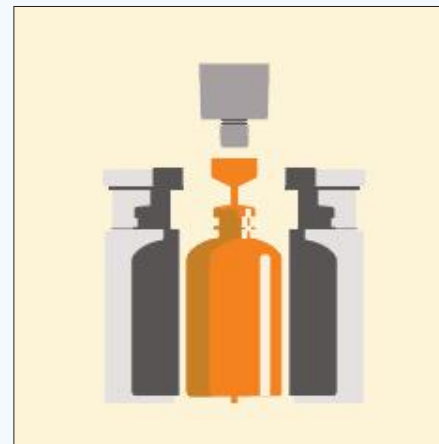
4 Aseptic Filling

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.



5 Aseptic Sealing

Mandrel is removed; head mold closes to seal the top of the plastic container.



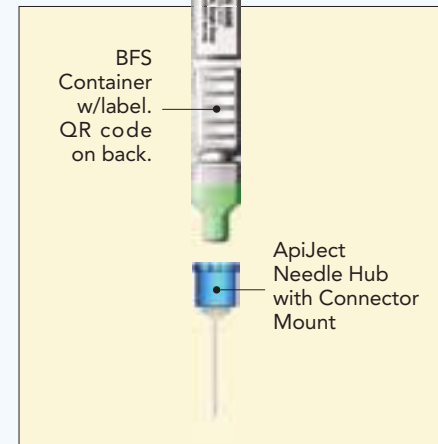
6 Trimming and Cutting

A continuous belt of prefilled containers scrolls out of main machine into the adjacent machine where excess plastic is trimmed off ("deflashed").



7 Inspecting

ApiJect containers are laser-inspected for stability and leaks. Required labels and VVMs, if needed, are then applied.



8 Pre-assembly

Sterile syringes move into a separate machine onsite for pre-assembly with connector mounts and Needle Hubs (previously manufactured offsite).



9 Wrapping and Packaging

Finished, prefilled syringes are wrapped & packaged for shipment, using standard automated systems for blister pack or ribbon pack containers.



The ApiJect System's "Soft" Syringe – a Wide Range of Uses and Global Impact

20-50% lower Total Cost of Delivery than a 10-Dose glass vial with better coverage, equity, speed and safety at no additional cost



Access for 400+ Million People

In many countries, vaccines and medications are wasted because there aren't enough medical staff to deliver them. Where permitted, ApiJect lets millions of health workers administer vaccines and medicines to millions of children, new mothers and adults.⁸⁰



Oxytocin and Hep-B at Childbirth

In the developing world, millions of women give birth with no medical professional present. As a result, every day approximately 830 women die from preventable causes related to pregnancy and childbirth.⁸¹ ApiJect could be used to administer low-cost Oxytocin to save lives.



Wider Use of Contraceptives

Many societies discourage contraception for social or religious reasons. Taking pills at home is highly "visible," so many women don't do it. With discreet quarterly self-injection, more women will be able to control their reproductive choices.



Faster Action in Medical Crises

Epidemics require rapid response. Making glass vials requires a lead time of up to 6 months or more.⁸² ApiJect's 1-2 month speed to market means much faster delivery of vaccines or medicines at scale.



Fast Help for First Responders

Soldiers, police and firefighters don't always have a medic, doctor or clinic nearby when injury occurs. ApiJect enables them to carry medicine for injection, enabling immediate treatment.



New Polio Vaccines

WHO has called for a global changeover from oral to injectable polio vaccines. When that transition occurs, ApiJect can support smaller doses where a formulation exists for ID injection.⁸³



HIV PrEP

New injectable HIV therapeutics are now in development that will require injections every month instead of daily therapies. The option for self-injection or injection by community health workers dramatically expands access.



Higher Flu Vaccination Coverage

About 60% of adults don't get flu vaccine injections in the West; coverage rates are even lower in other regions.⁸⁴ ApiJect's low-cost, potentially universal coverage and option (in low-resource counties) for self-administration can greatly increase vaccination rates.



Better Adherence Opportunities

For people who require ongoing self-injection of drugs or biologics, ApiJect can make adherence more likely because of its simple delivery system.



Allergies and Anti-Opioid Applications

Epinephrine and Narcan are very expensive in today's formats. IM injections using ApiJect requires smaller doses and offers a far less expensive alternative format.



ANIMAL HEALTH

Animal Health on Small Farms

Worldwide 70 billion farm animals are raised for food.⁸⁵ In low- and middle-income countries, far fewer farm animals receive medicinal injections than in the West. ApiJect can help small subsistence farmers and disadvantaged families treat animals showing signs of illness.



Veterinarians and Pet Owners

Veterinarians spend much time dosing injections for the world's 500+ million pets.⁸⁶ ApiJect eliminates that step, saving time. And, when veterinarians have the option to prescribe injections for pets that are given by owners at home, more pets will get treated.

ApiJect's Global Network of Established Suppliers

Each year, 50 billion units of plastic “squeeze bottle” containers are sold worldwide for sterile eyedrops, nose sprays and eardrops.

These containers are aseptically made, filled and finished using an efficient, low-cost plastics technology called Blow-Fill-Seal (BFS).



ApiJect uses BFS (Blow-Fill-Seal) aseptic plastic manufacturing.

Now a prefilled syringe can use this high-speed, high-volume process.

MANUFACTURE & LAUNCH

Established UNICEF & National Suppliers to Provide Global ApiJect Support at Launch

ApiJect has affiliated with 2 of the largest UNICEF-approved syringe manufacturers, as well as BFS leader Rommelag, to provide high-volume, high-quality, low-cost supply.

To build out a global network of manufacturer suppliers, ApiJect is entering into affiliation agreements with several well-established syringe manufacturers, including UNICEF's largest supplier of disposable medical devices, HMD Healthcare, and one of the world's most advanced needle manufacturers, Tae-Chang Industrial. They are joined by OneJect, Indonesia's leading distributor for government vaccine and family planning programs.

The leaders of these organizations have market-based experience in initiating new technologies and products that have become standards industrywide. Each understands the importance of keeping costs sufficiently low to support Gavi's goals of global coverage and equity, as well as the importance of conforming to WHO, ISO, EMA and FDA standards. These initial ApiJect suppliers have an established track record of serving markets at both national and global scale.

These three founding affiliates will be joined by Rommelag, headed by industry visionary Bernd Hansen, the world's leader in BFS. Rommelag's new \$50 million Swiss facility provides a state-of-the-art contract-fill solution.

In addition, FMW Group, led by partner Tobias Wilke, will provide world-class injection molds to ensure ApiJect's quality is upheld to the highest standards

Recognizing the importance of region-specific custom design, this manufacturing and distribution base enables ApiJect to reliably supply buyers in more than 80 nations in a timely manner while incurring minimal shipping costs.



ApiJect founding affiliates are ideally located to serve 85% of the population of low- and middle-income country markets.



ROMMELAG
Bernd Hansen
CEO

Switzerland: Rommelag, while not currently a UNICEF supplier, meets identical quality standards. Its 1,800+ employees serve customers in more than 80 countries around the world. It currently delivers vaccines and medicine in BFS packaging.

Rommelag is committed to provide contract BFS fill support and BFS machine sales to manufacturers. The company's contract manufacturing subsidiary has invested \$50 million to build a new BSL-2 filling plant in Zell, Switzerland. The Zell facility is in full operation currently and will support ApiJect.

Bernd Hansen's father Gerhard Hansen was the inventor of the Blow-Fill-Seal technology and founder of Rommelag in 1964. After studying electrical engineering, Bernd joined Rommelag in 1981 and became its CEO in 1985.



HMD HEALTHCARE
Rajiv Nath
Joint Managing Director

India: ApiJect will design its products specifically for the Indian, South Asian and Southeast Asian markets in cooperation with HMD Healthcare (Hindustan Medical Devices), one of the world's five largest syringe suppliers.

HMD has been manufacturing and supplying medical disposables for more than 60 years. Some 3,500 HMD employees at seven plants across South Asia supply more than 60% of India's disposable syringes, while producing more than 3.5 billion needles.

The Joint Managing Director of HMD's Hindustan Syringes & Medical Devices Ltd. is Rajiv Nath, who also serves as President of the All India Syringes & Needles Mfg. Assn.; and is the Founder and Forum Coordinator for the Assn. of Indian Medical Device Industry (AiMeD).



TAE-CHANG INDUSTRIAL
Hanjin In
Chairman

South Korea: Tae-Chang Industrial Co., Ltd. of South Korea is a global manufacturer of needle products, all of which are GMP, ISO & CE certified. Established more than 25 years ago, T-C Industrial exports to more than 50 nations, including the U.S. and Japan. The company's product development team and facilities supply global clients while serving as an OEM supplier to all major medical suppliers in the region.

T-C Industrial's next plant – its sixth – will be a 150,000 sq. ft. facility dedicated to ApiJect production, equipped with BFS machines for manufacturing and filling of BFS vials, through to final assembly with ApiJect hubs and sterilization.



ONEJECT
Jahja Tear Tjahjana
Chairman

Indonesia: OneJect Indonesia employs more than 300 employees in its 53,800 sq. ft. facility, housing manufacturing, engineering and R&D for medical devices. Established in 2004, OneJect is Indonesia's exclusive licensee for Marc Koska's K1 Auto-Disable syringe. Though not currently a UNICEF supplier, OneJect is Indonesia's largest distributor for government vaccine and family planning programs and is supported by Gavi.

Chairman Jahja Tear Tjahjana founded OneJect's original parent company, a general services contractor, in 1990. By 1994 he had expanded the company into large-scale infrastructure construction (public housing, airport facilities, etc.). OneJect is among a dozen companies that Mr. Tjahjana has launched or acquired since 1990.



FMW GROUP
Tobias Wilke
Partner

Germany: FMW is a developer of fine plastic products and a creator of the highest standard molds, which includes prototype, pre-production and serial production molds. They serve customers across the globe and in a variety of industries, including Medical Devices, Automotive, Packaging and Baby Products.

The FMW Group's three partners (Bernd Mohr, Stephan Fischer, Tobias Wilke) have each spent more than 20 years as senior executives or owners of larger globally active companies in the plastics (injection molding) and the toolmaking industries.

FMW is the inventor of various "safety caps" for standard syringes, including the "F Series." These are distributed by a partner worldwide under license.



MANUFACTURE & LAUNCH

ApiJect's "Process Architecture" Supports Pharmaceutical Companies in BFS Manufacturing, Filling and Finishing

We enable pharma companies to smoothly add established BFS methods and materials as a new packaging option to glass vials.

In addition to inventing a new "soft" syringe that represents the next-generation cPAD, ApiJect Systems has also invented a "process architecture" to support pharmaceutical companies that want to package their medicines and vaccines in ApiJect prefilled syringes.

This "process architecture" will provide a gradual, economical and logistically comfortable path that enables pharma companies to smoothly change over from traditional syringes and glass vials to BFS manufacturing.

The name of our process architecture is "BFS Fill and ApiJect Finishing," or BFAF. When a customer such as a national health ministry wants a certain drug delivered to them in the ApiJect form factor, the pharma company that manufactures that drug will decide among three options:

1. Buy the BFS equipment to manufacture, fill and finish the package themselves.
2. Rely on a 3rd-party Contract Manufacturing Organization (CMO) for both fill and finish operations.
3. Hybrid model: a pharma company could purchase a BFS machine to manufacture and fill their BFS containers but hire a CMO to run that equipment under contract in the CMO's outside facility. This allows equipment to be moved at a future time.

CMO finishing operations will include testing the filled BFS containers; pre-attaching mounts and Needle Hubs with the proper sized, double-ended needle for each



drug or vaccine; laser-checking the combined unit to ensure stability and lack of any leakage; then wrapping, boxing and shipping.

BFS manufacturing equipment costs about \$10 million for a single packaging line that can produce 200+ million BFS containers per year. Because today's pharmaceutical companies typically use proprietary glass filling plants, they do not currently own BFS machines and the required finishing equipment.

Accordingly, until demand for ApiJect is strong enough for pharmaceuticals manufacturers to justify investing in their own BFS equipment, they are likely to send their drugs and vaccines to our CMO partners.

MANUFACTURE & LAUNCH

ApiJect Will Establish a Dedicated Global Network to offer "BFS Filling, ApiJect Finishing" Options

Starting in 2020, new facilities will be constructed to serve as "BFAF" Contract Manufacturing Organizations in Asia and Europe.

ApiJect and its South Korean partner Tae-Chang Industrial Co., Ltd. are building the first fully integrated, end-to-end, vaccine-ready BFS Filling & ApiJect Finishing (BFAF) line for vaccines.

Designated "Facility Zero," it is the first in a planned global network of dedicated facilities that will both manufacture BFS containers, ApiJect Needle Hubs and connector mounts, and provide the necessary filling and finishing services, all within the cold chain whenever needed.

ApiJect's "BFAF" network will support pharmaceutical companies worldwide on a CMO (Contract Manufacturing Organization) basis.

Breaking ground in the fall of 2019, Facility Zero will begin with a single BFS line that is capable of manufacturing 200+ million BFS syringes per year.

Space, power and other logistical factors in Facility Zero will support a total of six BFS production lines, bringing the plant's annual production capacity to 1.2 billion or more ApiJect units per year as demand increases. Facility Zero will be certified by the South Korean Ministry of Food & Drug Safety.

Several additional ApiJect suppliers have agreed to be part of our BFAF CMO network. Rommelag will build BFAF Facility One in Germany or Switzerland.

T-C Industrial, Rommelag and other ApiJect suppliers are already well-established in their respective markets

and are capable of efficiently serving their global regions.

T-C's blueprints for Facility Zero will enable other ApiJect supplier partners to replicate the plant, increasing speed and efficiency of the construction phase for Facility One, Facility Two, and beyond.

Each drug or vaccine will receive the required, separate regulatory approvals to be manufactured in BFS syringe format; filled in a given facility; and finished in the same or another facility.



ApiJect's 31 "Soft Benefits" are Difficult to Measure in Dollars, but Improve Lives in Many Ways

The benefits of a BFS "soft" syringe cannot be assigned a specific monetary value – but they still provide meaningful real-world quality-of-life improvements.



1. Much better coverage and equity

Improves delivery of injectable medicines and vaccines to 400+ million patients in remote places, far from medical staff and clinics.

5. Injection speed

Health workers can inject more patients in less time, especially in mass vaccination settings. This is especially important when time is limited in crisis situations.

6. Perfect dosage accuracy

A BFS machine perfectly fills the ApiJect container every time, eliminating the chance of over- or under-fill.

7. Less overfill

Precise prefilling requires less overfill per dose than the normal 10% per vial.



11. No reuse possibility

Single-use feature prevents reuse, reducing spread of disease.

12. No risk of glass flaking contamination

All medical-grade plastic device eliminates contamination of medicine from glass flaking and thus no glass-based recalls.

16. Less training

Fewer steps mean less training for almost anyone to use. Ideal for optional self-administration, especially in contraceptive use.

17. Less fear

Smaller device and ID needle options creates less patient anxiety. More adoption & adherence.

18. Lower needlestick risk

PATH study of cPADs shows smaller format means less chance of accidental needlestick.



23. Small manufacturing footprint

BFS technology is small and efficient. A \$5M machine capable of delivering 200 million doses a year fits in a shipping container and can be set up in any suitable location.

24. Pocket portable

Device is sufficiently small, light and sturdy – able to be carried in a pocket without breaking.

28. Less pain

Patients prefer shorter needles. Fear of pain and needles prevents many patients and parents from getting urgently needed injections.



2. CHW empowerment

Millions of community health workers and midwives – with governmental approval – can now give injections because of the ease of the process.

3. Self-injection option

Patients can self-inject with success and confidence, where appropriate and approved (e.g., contraceptives).

4. Labor utilization

No time is spent filling syringes from vials – enables more efficient routine use of nurse labor.



8. Reduce human error

Color-coded syringes are easy to read. Labels show user which drug and dosage is contained in the ApiJect prefilled syringe.



9. Fractional dose option conserves vaccine supply

In situations where certain vaccines are in short supply, syringes can be prefilled with fractional ID doses, increasing coverage and the number of lives saved.

10. Intradermal/subcutaneous needle optionality

Prefilling does not require fluid withdrawal from a glass vial using long needles. ApiJect is prefilled and supports even the shortest intradermal needle.

13. Minimizes drug waste

Single-dose, prefilled container reduces "extra" medicine being thrown away unused or expired. This is most valuable in countries with high volumes of drug wastage from 10-dose glass vials.

14. Drone delivery optionality

Doses can be safely airdropped without special packaging or breakage.



15. Less total weight and volume

Glass is heavy and more difficult to carry and transport. Plastic is light and far more doses can be carried by a person, especially a medic or CHW on foot or in small vehicle.

19. Pandemic response time

Speed to market is much faster than glass vials and can get large quantities of a vaccine from factory to the public in days or weeks.

20. Adherence

Because the format is easier to use with less fear, patients are more likely to stay with longer term treatment regimens such as allergy injections, HIV, etc.

21. Pandemic coverage

Allows faster, wider vaccinations of more people, by more people.

22. Anti-counterfeiting

Simple 2-second scratch-test shows product is genuine and can be trusted.

25. Animal use option

Device can be used for critical small animal needs, especially in areas with low veterinary coverage.

26. Environmental impact: energy and materials

Uses less energy and raw materials in manufacturing.

27. Environmental impact: less disposal waste

Creates less waste after device is used.



29. Environmental impact: far less pollution

BFS manufacturing creates far less pollution and far less waste byproducts compared to glass.

30. No glass breakage waste

Zero glass breakage in manufacturing or transit. Less cost. More coverage.

31. Real data, real time

Optional NFC tag version generates dose-level point-of-care reporting, giving an overview of coverage rates by location.



To learn more about ApiJect's benefits, read our booklet "ApiJect's 32 Soft Benefits are Difficult to Measure" or download it at bit.ly/apiject-red-booklets.

MANUFACTURE & LAUNCH

The ApiJect System: Components and Regulatory Approach

ApiJect’s system combines a wide range of different containers, Needle Hubs and VVM options. This drives a component-based registration process.

Modularity is the traditional approach for injectables technology. For more than a century, needles of many lengths and sizes have worked interchangeably with a wide range of vials and syringes to bring vaccines and medicines to the world. The ApiJect System is a family of new products that updates this modular approach with a variety of new designs and proven materials, while preserving the same underlying philosophy of standardized, interchangeable parts.

The ApiJect System includes multiple Needle Hubs with typical needle lengths. These hubs use a standardized interface to marry individual needles to BFS containers – the “packaging” for injectable vaccines and medicines.

All ApiJect System products are shipped in sealed foil packages. Needle Hubs can be pre-attached to sealed BFS containers but are not pre-activated. That is, the double-ended needle does not pierce the container holding the medicine or vaccine until the end user deliberately presses the components together, immediately prior to injection.

Modular design greatly increases design flexibility

ApiJect’s modular design offers enhanced flexibility at lower cost.¹¹⁹ For traditional injectables technology, i.e., glass vials and traditional syringes, the mix-and-match utility creates a limited degree of flexibility.¹²⁰ This is due to the economics and manufacturing limits of working with glass. Once certain sizes, shapes and components

have become standard (i.e., one-dose vials, 10-dose vials; etc.), large sunk costs and long lead times make it prohibitively expensive to reconfigure the manufacturing process for new designs. In practical terms, these limits on glass manufacturing flexibility also limit the opportunities and incentives for innovation, customization, and variability. Economic reality and practical necessity force suppliers and users to make do with the status quo decade after decade.

The ApiJect System overcomes these limitations

The ApiJect System economically supports design and manufacturing customization, innovation and variability. With BFS, creating a new module for the ApiJect System – such as a new BFS container – merely requires refitting an existing manufacturing machine with a new mold.¹²¹ Consequently, innovation becomes fast and affordable. In fact, innovations can even trigger cost reductions.¹²²

A new world of opportunities

The ApiJect System makes full use of mix-and-match modular design. Pharmaceutical companies will pair any of three needle sizes with our dual-chamber BFS container to deliver vaccine or medicine. In a few years, we expect the ApiJect System will include a variety of Needle Hubs and dozens of different BFS containers that are ready to be approved by regulatory authorities when used with a specific drug. Pharmaceutical companies can then pair any Needle Hub with a BFS container in a shape of their choosing to create a combination that best meets their needs. Options are also available to add Vaccine Vial Monitors to the BFS container (indicates whether vaccine has been kept at proper temperature) and, soon, RFID chips for injection tracking.

A new way of thinking about injectables technology

The ApiJect System represents more than simply a new product or even a new manufacturing technology. It is a new way of thinking about delivery systems for injectable vaccines and medicines, limited only by our imaginations.


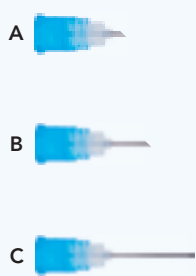
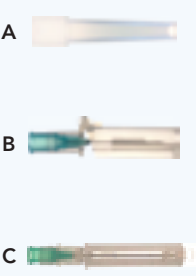


ApiJect's regulatory approval pathway

Every time a drug is filled in an ApiJect device and offered in a new market, ApiJect and its pharmaceutical partner will pursue a “combination” device approval strategy.

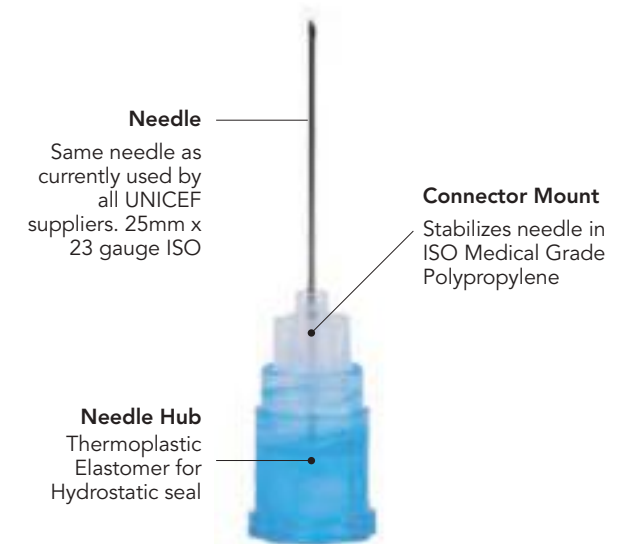
- 1. Needle Hub:** ApiJect will get regulatory approval for its Needle Hub. This is well-predictated technology.
- 2. BFS Container + Drug:** The pharma company will fill our BFS container with its drug and perform compatibility and stability tests to ensure there is no interaction between the plastic and the drug.
- 3. Combination:** The approved Needle Hub and the approved BFS container/drug will be attached and submitted to regulators as a combination device.

This process will be followed in all markets. WHO will require one more step of additional regulatory approval before they grant PQS approval to our device packaged with a specific drug.

The ApiJect System: An ever-expanding set of safe, low-cost injection options

| BFS CONTAINER DESIGNS | APIJECT STERILE NEEDLE HUBS | SAFETY CAP CHOICES | PRE-ATTACHED 10-STRIPS (non-activated) | OUTER PACKAGING |
|--|---|--|---|--|
|  <p>Illustration only</p> |  |  <p>Illustration only</p> |  <p>Combination product: Needle Hubs and BFS containers</p> |  <p>Outer foil wrapping options</p> |

The ApiJect Needle Hub



Making mono-dose injection formats available at the lowest cost per dose will provide cost and time savings throughout health delivery systems and supply chains, while supporting greater coverage and equity of access in the last mile.

FAR-REACHING IMPACT

SECTION 6

Serving More Patients With the Same Budget & Staff



**ApiJect supports global public health
with a wide range of uses.**

**Worldwide, every child and new mother
can get the life-saving injections they need.**

FAR-REACHING IMPACT

Global Health in its Many Forms

ApiJect represents an entire platform change for injectable medicines. The following are some of the areas where ApiJect can make a real difference.

Pandemic Defense

The next mass-casualty pandemic is not a question of “if,” but “when.” And governments do not have the fill-finish capacity to adequately protect their citizens. By working in a public-private partnership with governments, ApiJect can help ensure that health ministries are able to respond as quickly as possible to immunize their populations against the threat.

At 21 million doses per BFS machine per month, ApiJect has the surge capacity to get vaccines and medicines to first responders in a timely fashion.

And, if BFS manufacturing facilities are ready to respond rapidly to such emergencies, ApiJect devices can start being manufactured within just hours of the drug being delivered in a bulk format.



Injectable Contraceptives

According to the UN, 758 million women ages 15 to 49 who are married or in a relationship practice family planning.¹⁶⁵ Injectable contraceptives are the third most popular form of non-permanent female contraception, and the fastest-growing of the major methods. Yet lack of access to medical care means another estimated 143 million women cannot practice pharmaceutically-based contraception.¹⁶⁶ ApiJect can help them. Its low cost and high-volume manufacturing capacity can allow NGOs and health ministries to make injectable contraceptives more widely available to their at-risk populations.

A single injection remains effective for 2-3 months, making it a convenient option for most women. And, with its compact size, ApiJect can be stored discreetly at home and used as needed by many women who do not have easy access to a health clinic for regular injections.

Oxytocin and Epinephrine

Last year, according to the WHO, an estimated 70,000 mothers died from blood loss during childbirth. For many, their lives could have been saved if they had access to a standard injection of Oxytocin during the birthing process.

This inexpensive hormone is a staple in nearly all modern hospital births in high-income countries. Unfortunately, many of the 90 million mothers who give birth annually in low- and middle-income countries do not receive Oxytocin and are consequently at risk. Likewise, Epinephrine is a hormone that saves people who are suffering from a life-threatening allergic reaction. Examples include anaphylactic shock resulting from a bee sting, or a severe asthmatic reaction to food, triggered by an allergy. However, the market cost of Epinephrine makes it prohibitively expensive for millions of people who need to have it readily available. ApiJect’s low cost and ease of rapid-scale manufacturing can make it affordable and practical for millions of people to receive emergency injections of these and other hormones. ApiJect’s compact size and ease of use also make it ideal to keep on hand for at-risk populations.



Tuberculosis Test

In 2018, there were 10 million new cases of Tuberculosis (TB) – and the number is growing. When there is a TB outbreak, governments and NGOs try to act quickly to contain the disease. Unfortunately, the cost of treatment is high. Ideally, to save money and limit the number of patients, members of at-risk populations should be given a screening test that helps health professionals assess the likelihood that a specific individual is developing TB. The difficulty is that the TB test requires an intradermal (ID) injection, and since most ID injections are given with longer intramuscular needles, only a trained professional can administer them. (Shallow injections made with long needles require the administrator to use the Mantoux method, which requires skill and practice.) ApiJect helps alleviate this problem. The device can be equipped with an ID Needle Hub, allowing for a standard – and much simpler – injection technique, not the Mantoux method. This makes it possible and practical for a larger population of healthcare professionals to administer the needed test. Furthermore, ApiJect’s low cost means that governments can procure more TB tests on the same budgets.



To learn more about the potential impact of a single-dose format like ApiJect, read our booklet “Injectable Contraceptives Not Only Improve the Health and Lives of Women, but Transform Communities” or download it at bit.ly/apiject-red-booklets.

FAR-REACHING IMPACT

ApiJect's Prefilled Syringe Can Significantly Reduce Labor Expenses by Saving Nurses' Time

Preparing injections with prefilled syringes is up to 39% faster¹³⁹ and giving injections is nearly 50% faster.¹⁴⁰



For tens of millions of nurses in hospitals and clinics, preparing and giving medications is a large part of their daily duties. U.S. nurses can easily spend up to 27% of each workday on the protocols required for what is known as the "Medication Administration Process."¹⁴¹

This process begins with information retrieval and managing physician orders. It continues with obtaining, verifying, preparing and delivering meds, and ends only when nurses perform data entry for all required follow-up documentation for each medication given.

Injections typically account for 45% of all medications given to patients at hospitals.¹⁴² (Many hospital injections are given through an IV drip and hep lock or catheter, but nurses still utilize a syringe to transfer these meds into the IV solution.)

Preparing all those injections – finding the right vials,

laying out syringes, filling syringes from vials, etc. – can be a time-consuming task all by itself.

Using prefilled syringes creates meaningful time savings for nurses, both in preparation and delivery of injections. Staff can save 27% to 39% in preparation time with prefilled formats compared to vial formats, since it eliminates the task of filling syringes from glass vials.¹⁴³

As for actually giving an injection of medicine or vaccine, this task can take 46 to 65 seconds with a vial and traditional syringe, compared to 29 to 48 seconds with a prefilled syringe...nearly 50% faster with prefilled formats than with vials.¹⁴⁴

When multiplied across 10-14 injections per patient, per day in clinical settings in high-income countries,¹⁴⁵ these time savings can drive significant labor efficiencies and cost reductions for healthcare organizations.

FAR-REACHING IMPACT

Medication Errors and Resulting Adverse Drug Events (ADEs) Can Be Significantly Reduced with ApiJect

Injectable medications are associated with preventable ADE's in 1.2 million U.S. hospitalizations each year (\$5.1 billion), and far more on a global basis.¹⁴⁶

When a nurse gets interrupted while preparing medications for injection – a frequent occurrence, according to numerous studies – results can range from dosing errors to vial mix-ups, so that a patient receives the wrong medication.¹⁶¹

Medication administration errors in hospitals in high-income countries reportedly take place with 1 out of every 5 medication doses.¹⁴⁷ These errors are dangerous to patients and costly for healthcare organizations. Medication errors result in some 7,000 deaths per year in just the American healthcare system.¹⁴⁸ The typical U.S. hospital pays \$600,000 per year to cover liability exposure for preventable Adverse Drug Events (ADE), according to the American Nurses Association.¹⁴⁹

What's more, the actual total cost of ADE's across the U.S. hospital system may be significantly higher, since



6 out of every 7 hospital-based errors, accidents and other adverse events goes unreported, according to U.S. Department of Health and Human Services' Office of the Inspector General.¹⁵⁰

Prefilled syringes such as ApiJect can reduce or nearly eliminate injections of the wrong medicine or dose. Nurses reduced medication error rates from nearly 75% with vials to single digits with prefilled formats in one study.¹⁵¹ In another study, paramedics reduced critical dosing error rates in emergency simulations from 39% with vials to zero (0.0%) with color-coded, prefilled syringes.¹⁵²

For hospitals struggling to control costs, ApiJect prefilled syringes can reduce error rates and ADEs, which translates into fewer patient harms and less cost for liability exposure.

FAR-REACHING IMPACT

Introducing ApiJect/Vet: “ApiJect for Animals” A prefilled Mono-Dose for Pets and Animal Companions

Worldwide, pets receive an estimated 500 million injections per year; ApiJect means faster, safer, more convenient and lower-cost care.



Both veterinarians and pet owners will benefit from an easier, simpler, lower-cost option for injections.

An estimated 400 million dogs serve as animal companions to humans worldwide. In the U.S. alone, the pet population includes more than 70 million dogs; the number of cats is higher. As nations grow their GDP, pet healthcare and pet spending grows along with it. In the U.S., pet owners spent an estimated \$69 billion on acquiring, feeding and caring for their pets in 2017.¹³⁶

The animal health market in the U.S. commands its own \$26 billion economy; total U.S. pet industry expenditures were expected to reach more than \$72 billion by 2018.¹³⁷

We estimate there are half a billion injections per year that serve the world's population of companion animals, and the number is growing rapidly. ApiJect can make it easier for veterinarians to vaccinate pets with our low-cost format, provided to the pet and animal companion

market with a specialty version of the ApiJect product called ApiJect/Vet.

Our prefilled presentation will be welcomed by veterinarians. As mentioned previously, according to time and motion studies by PATH, prefilled syringes enable injections to be given in half the time required to use traditional syringes and glass vials.

Even more time is saved in preparing lyophilized (dry powder) vaccines that must be reconstituted with liquid before injection, a format used for many animal medications and vaccines. A future version of ApiJect/Vet will be prefilled with both the powder and the liquid diluent for rapid and foolproof reconstitution. Vets will be freed to spend more time on their patients and less time preparing injections.

FAR-REACHING IMPACT

ApiJect/Vet Can Also Help Subsistence Farmers Worldwide Keep Livestock Healthy – and Keep Families Alive

Most animals on small farms go unvaccinated, putting livestock and farm families at risk.

Hundreds of millions of small family farms around the world keep livestock, from dairy cows and goats to sheep and poultry. For billions of people in many Low- and Middle-Income Countries (LMICs), these animals serve as a major protein food source and generate critically needed income from valuable products such as meat, wool, hair, silk, hides, skins, furs, wax, feathers, bones, horns and more.

At the same time, these “living renewable resources” often provide the chief means of physical survival for many families on small farms, serving as their primary source of food since animals produce meat, milk, eggs, and additional edibles. If farm animals in these sectors get sick or die, the humans who own them can be at risk, too – not just for adverse health impacts, but for the family's physical survival. Unfortunately, in much of the world,

most of these animals go unvaccinated. The UN estimates that only 38% of livestock in Tanzania and 21% in Uganda receive vaccines; similar numbers are treated for parasites and other infections.¹³⁸ Low rates of basic animal healthcare often result from limited availability of injectable medicine and vaccines; and, unsustainable high costs.

Through its ApiJect/Vet product line, ApiJect's low-cost, high-volume, versatile and easy-to-use technology could have a significant impact on this enormous, often overlooked, segment of global health. By making it both convenient and cost-effective for hundreds of millions of subsistence farmers and small farmers worldwide to treat their livestock, ApiJect/Vet enables small farm animals to safely generate more income and more sustenance, ultimately improving the family's well-being.



ApiJect can be fitted with small needles for small animals with soft skins, or with the larger needles to pierce thicker hides.

Mobile phones and wireless networks have transformed the world. Globally, there are now more mobile devices than people.

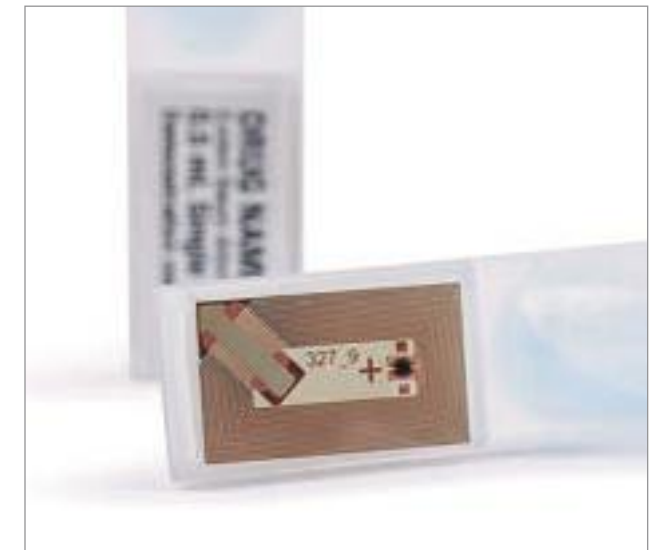
ApiJect offers the option of a low-cost computer chip that sends information from each dose through mobile phones and integrates with the Internet of Things, enabling health organizations to track billions of injections in a new way that will accelerate health systems strengthening.

As mobile continues to improve the everyday lives of ordinary people, data-driven planning and decision making becomes the critical frontier in global health.

INJECTIONS ON THE IOT

SECTION 7

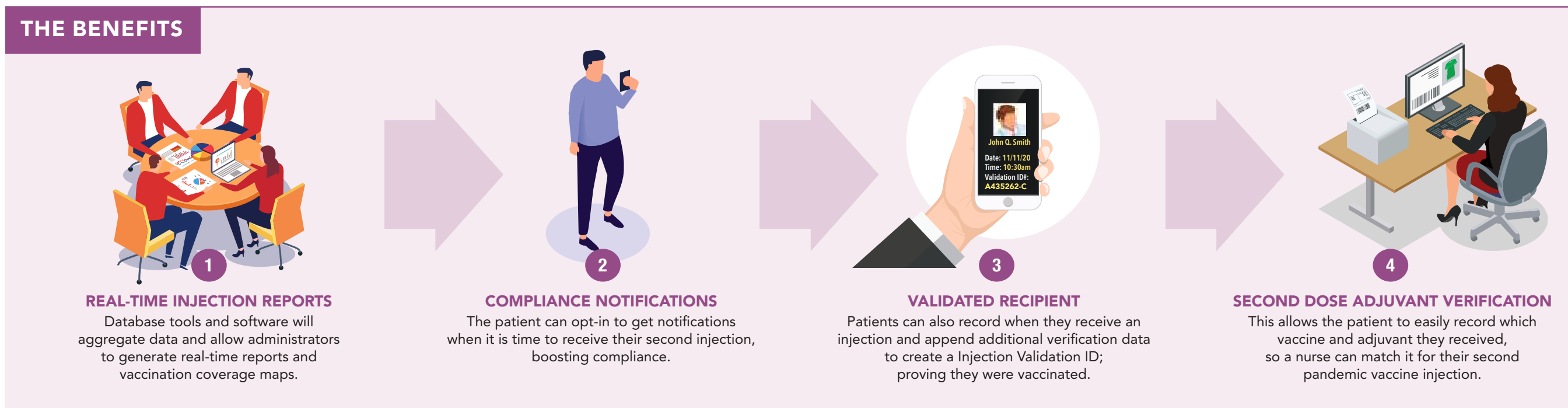
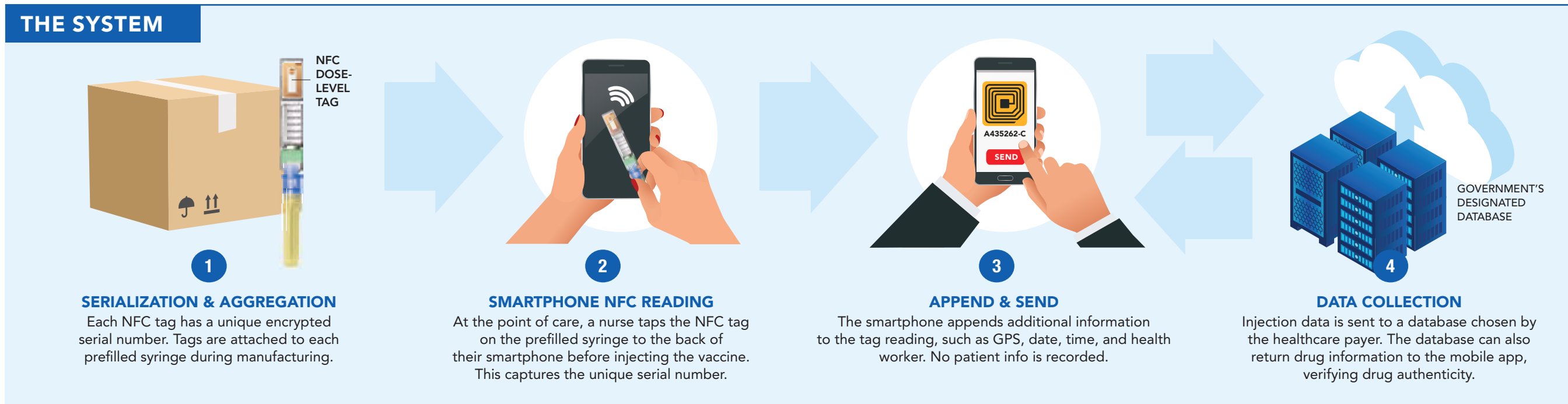
Putting Medical Injections on the “Internet of Things”



A built-in RFID chip is optional on every ApiJect prefilled syringe. Result: real-time remote tracking of all injections is now possible.

Overview of Dose-Level, Point-of-Care Tracking Technology for Pandemic Scenarios.

How low-cost, dose-level tracking using NFC tags on each BFS prefilled syringe would work.



INJECTIONS ON THE IOT

ApiJect will be the first unit-dose format that allows every injection to be tracked on the Internet of Things

Mobile phones and data networks are the defining tool of our time. Putting injections on the Internet of Things will help provide 100% injection coverage, equity and safety.

The Problem:

With billions of injections given per year, the world's medical organizations, communications technologies and reporting protocols cannot be expected to accurately track who gets what injection of medicine or vaccine.⁸⁷ Add the variables of when, where, who delivered it and the lot number of each particular dose and the problem of gathering timely data is even harder. When it comes to tracking and measuring vaccine coverage, too often the global public health and healthcare communities are "flying blind."

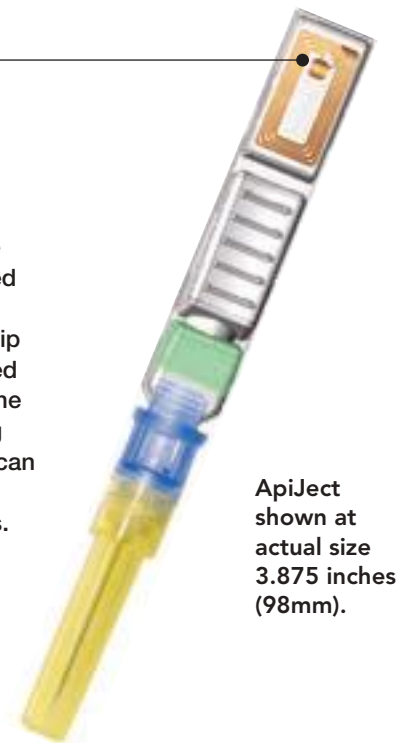
Even the most ambitious and well-funded campaigns to bring vaccines and medicines to the world, find it difficult to measure their success rates and target under-performing areas for improvement. Planning suffers when there is a lack of fast, accurate, actionable data. Short of spending billions of dollars on new technology, how can

we build a simple (yet also modern) data ecosystem that can instantly track all injections of vaccines and medicines anywhere in the world...one dose at a time or millions of doses in weeks?

The Innovation:

In 2021, ApiJect will be the first to offer an affordable, effective solution using a suite

In Phase 2, ApiJect adds a low-cost passive RFID NFC chip with a unique ID# embedded at the time of filling. The chip can be located underneath the required drug labeling and can also be used on glass vials.



ApiJect shown at actual size 3.875 inches (98mm).

of technologies that will add a new option for health data communications. The resulting platform weaves together current mobile networks; the Internet of Things; the GPS network; widely established radio-frequency ID technology (RFID) and the existing global mobile/ computer network. It will enable ApiJect to capture and instantly generate an automated report with accurate data about every ApiJect injection given in the field to public health officials or organizations such as Gavi. The resulting data can then be distributed to all stakeholders.

The Technologies: RFID and NFC

Each Phase 2 ApiJect device can be manufactured with a Near-Field Communications (NFC) chip embedded in the plastic hand grip of the syringe. It is the same type of RFID chip found in billions of credit cards, debit cards and modern smartphones all over the world.

Unlike a QR code, each self-contained chip actively and continually broadcasts data, and can be remotely queried (even inside a closed box). It costs just a few cents per unit based on data size requirements.⁸⁸

NFC chips are what engineers call "passive devices," which means they do not need or contain an internal power supply. Instead, the chip is activated when it comes within a few inches of an outside power source, such as the antenna embedded in a mobile phone.⁸⁹

Each NFC chip will store a unique serial number. When that number is uploaded to the cloud, it is instantly associated with a data set of 8 essential identifiers.

The Process:

To activate ApiJect Phase 2's automated reporting data feature, a health professional or community health worker (CHW) performs 3 simple steps:

1. Launch the ApiJect app on their mobile phone.
2. Tap the back of the phone to the ApiJect device so that the magnetic field activates the chip and captures the unique serial number. In a second, the number is captured and the phone screen confirms "Data Received."
3. Then the provider injects the vaccine or medication with the ApiJect device.

Non-personally identifiable data are automatically uploaded from the phone's app to the Internet of Things (in real time or batch delayed), where it is associated with a specific data set. This data is combined with data from other ApiJect devices in the field to generate useful reports for anyone who needs them.

The Data:

When the central data system receives the serial number from the ApiJect chip, it also captures associated time and geo-location data (GPS) from the phone.

The serial number and time/place data are then stored in a cloud-based system. The system knows:

1. The **specific drug** being administered (from the serial #).
2. The **actual dose** being administered (from the serial #).
3. **Location** where injection is given (from GPS).
4. **Time** when injection is given (from the phone's operating system).
5. **Healthcare professional** who gave the injection (from app & phone identifier).
6. **Clinic** where injection was given, if any (from GPS data interpreted from clinic mapping).
7. Manufacturing data and **history** of the drug, including batch number, manufacturing date, shipment history and destination, order number, customer number, delivery place and date (from serial #).
8. Ambient outdoor **temperature and weather** at the time and location of injection (from correlation of weather data with GPS location and time of chip activation).

Key Benefits:

Starting in 2021, ApiJect will be able to provide national and global health organizations such as Gavi and WHO with detailed, accurate, real-time snapshots of injection coverage and effectiveness. Data from millions of ApiJect devices can be compiled and aggregated in to useful reports on the trends and locations of coverage. All data can be accessed and incorporated into the WHO EVMA 2.0 Framework⁹⁰ at no cost.



India's software design industry will be a major contributor to ApiJect Phase 2 – adding the capability for mobile-based tracking for every injection

Every injection made with ApiJect Phase 2 will be able to easily transfer non-personally identifiable and aggregated critical health data in real time to global public health officials, using advanced technology that will be designed in India. ApiJect will rely upon Indian-based software engineering to co-design the hardware design and write the needed code base to drive ApiJect Phase 2.

ApiJect has both an in-house software facility in Delhi and will work with one or more of India's leading technology suppliers. India is a logical choice for two reasons. First, with a population of 1.3 billion people, India may be the world's largest market for medical injections, including vaccines and therapeutics, which ApiJect estimates adds up to billions of injections per year.

The second reason ApiJect has selected India's software industry to develop ApiJect Phase 2 technology is the nation's leadership in software development. Generating US\$120 billion per year



ApiJect will use the proven capabilities of 100+ developers who currently perform advanced code-writing in the Delhi based facility owned by the Walker family of companies.



India's Union Minister for Science & Technology and Earth Sciences, Dr. Harsh Vardhan, with Mr. YS Chowdary, Minister of State for Science & Technology and Earth Sciences and other dignitaries at a 2017 Biotechnology Industry Research Assistance Council event.

and employing 13 million people directly and indirectly, IT is India's fifth largest industry.⁹¹ The sector's reputation as a world leader in software development is unsurpassed. India's IT services for export are growing 9% per year while the domestic market is expanding 10-12% annually and India's digital services are growing twice as fast.⁹²

As of 2019, India's medical device industry is valued at US\$5.2 Billion and is growing at 15.8% CAGR; various sources project that by 2025, the market will reach US\$50 billion.⁹³

The nation's mHealth services are projected to grow just as rapidly, expanding from US\$435 million to US\$945 million by 2020.⁹⁴ In addition, the Indian healthcare IT market is currently valued at \$1 billion and is likely to grow about 1.5 times by 2020.⁹⁵

ApiJect has a dedicated software development facility in Delhi, that will be utilized to execute the engineering of its Phase 2 technology.

ApiJect will also forge several high-level partnerships with India-based producers of health related data. These companies will assist with aggregating and correlating data uploaded from ApiJect Phase 2 devices in the field, and translating that data into a wide range of actionable reports that will be supplied to healthcare organizations worldwide.

Medical organizations will receive detailed reports that answer questions such as:

- How many health workers and which ones, in which clinics of Region 9, participated in our Hep-B vaccination campaign this month? How many patients did each worker inoculate overall? Per day? Per week?
- Are routine weekly birth doses of Hep-B inoculations increasing or decreasing in Districts 27, 36 and 44?
- How quickly does Clinic #47 use up its polio vaccine after each new shipment? Should the volume and frequency of shipments be increased? By how much?
- How do inoculation rates with the new RSV vaccine in Clinic #214 vary with weather?

Users will be able to generate reports that answer these questions and thousands more. Health organizations will know where they are succeeding and where more effort and resources are required. They will be able to pinpoint high-level success zones as well as problem areas, and able to assess the reasons for each.

mHealth and the IoT: important new tools for strengthening health systems around the world

WHO has stated that mobile and wireless technology "has the potential to transform the face of health service delivery across the globe" and to effectively support widely shared goals of achieving greater global coverage and equity.⁹⁸

The mobile-connected technology of ApiJect Phase 2 falls within the broad field of "mHealth." WHO defines mHealth as a "medical and public health practice supported by mobile devices, such as mobile phones, patient monitoring devices, personal digital assistants, and wireless devices."⁹⁹

Today there is a high level of global enthusiasm about the potential of mHealth. Billions of dollars are being invested at all levels and across all sectors of the ecosystem. These levels and sectors include national health ministries; numerous regional organizations around the world; various

Millions of hotel rooms currently use RFID chip cards for "keyless" room entry

Who would have thought 20 years ago that the 6,000-year-old key would first be replaced by a mag stripe and door reader and then again by 10¢ worth of disposable, reprogrammable computer chip? That's exactly what happened.



RFID-enabled card keys have replaced the old metal keys in nearly every new hotel over the past decade. Together, with mag-stripe keys, digital keys are now the standard

for most of the world's 15+ million hotel rooms.⁹⁶

Today's "tap and go" card keys provide multiple layers of room access privileges (guest, housekeeping, security, fire, etc).

Billions of credit cards join the trend

RFID-based inexpensive NFC chip technology has expanded to credit cards and card reader

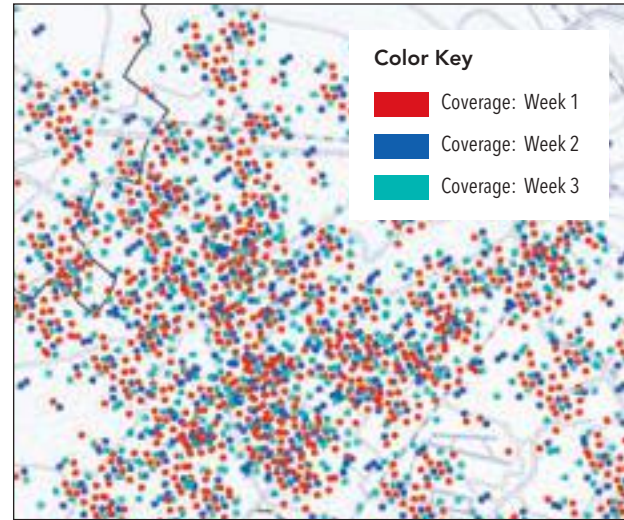


systems from Visa, MasterCard, American Express, Apple and Samsung.⁹⁷

RFID and related chips are now everywhere worldwide, from the local Starbucks to the millions of retail locations that now accept contactless payment options. It was just a matter of time before these same technologies became incorporated into health systems.



This 1854 London map was used by Dr. John Snow to track cholera cases and identify their source: a contaminated well.



ApiJect with digital network connectivity will enable health agencies to track injection rates and improve planning.

research and treatment efforts targeting specific diseases; hospital systems; pharma companies; medical device makers; and more.

As mHealth solutions demonstrate an ability to expand coverage and deliver more impact for each dollar spent, a growing appetite is expected for such solutions among health ministries in low- and middle-income countries, and payers and regional and global health organizations. These entities could benefit from IoT-connected support of their ongoing efforts to monitor and track vaccine and drug administration in the field.¹⁰⁰

ApiJect believes its Phase 2 technology will provide useful support to the coming explosion of mHealth use. Phase 2 is designed to address these critical needs through its functionality, which enables better monitoring and tracking of immunization and treatment campaigns in remote areas, and through its simplified operations.

ApiJect Phase 2 features open APIs, enabling all stakeholders to participate

Consistent with ApiJect's mission of global coverage, Phase 2 technology will feature an open API – a publicly available application programming interface. Developers from any qualified stakeholder, at any level of the health-care infrastructure, get full and free access to ApiJect's

aggregated data (including no information that could identify individuals).

ApiJect will furnish stakeholders with the ability to design their own national or international systems for compatibility and communication with Phase 2. They will also have the ability to modify and control their unique use of Phase 2 reporting and data transmission functions. And, they will have the ability to control access to data for their country or their specific target populations. All data acquired by ApiJect Phase 2 will belong to the country, payer or organization that manages or funds a particular program. ApiJect has no data ownership.

ApiJect Phase 2 will be useful to stakeholders at all levels in the health ecosystem

While ApiJect Phase 2 serves the healthcare system from the top down, it also serves participants from the field-level up. Clinic managers will benefit because Phase 2 will make it effortless to obtain comprehensive data on their clinic's performance right on their phone, with no paperwork, including comparisons to performance during previous periods, trend lines for coverage, and more. And, depending on the country, there is a broad range of logistics integration and support that will benefit from near-real-time, injection specific field data available on the IoT.

Global support infrastructure for mHealth is already widely available

WHO, anticipating the rapidly growing importance of healthcare organization-driven mHealth, directed its mHealth Technical Evidence Review Group to develop an mHealth evidence reporting and assessment (mERA) checklist that provides preliminary standards and guidelines.¹⁰¹

Global support infrastructure for mHealth is already widely available. WHO has tracked mobile subscription rates since the early part of this decade. Today there are more than seven billion mobile network subscriptions worldwide.¹⁰² As of 2011, WHO reported that over 70% of mobile subscribers resided in low- and middle-income countries.¹⁰³ The current rate is much higher.

Supporting this broad global base of mobile devices, a number of the world's leading technology companies have invested resources in developing and providing solutions for capturing and storing large volumes of health data, as well as analytics to and for stakeholders in the healthcare ecosystem, including pharma, payers, patients and more. Numerous high-tech corporations have established sufficient global penetration to enable them to provide scalable service, with programs, capabilities and appropriate privacy protections that can be customized for each country as it establishes its unique regulatory requirements.

ApiJect will seek design input for Phase 2 from Gavi, PATH, ministries and field-based CHWs

ApiJect seeks to work closely with Gavi, PATH, WHO, health ministries and NGOs "on the ground" to ensure that Phase 2 supports both medical professionals and non-professional healthcare workers in the field. That starts with Phase 2's simple mHealth technology: an RFID/NFC chip in each syringe that communicates with an app installed on any health worker's phone.

Equally simple will be the worker's role in activating

Phase 2's reporting. Just tapping the back of the phone to the syringe is the sole requirement. Data transmission, as well as subsequent report generation, are automatic. Technology experts have acknowledged that for patients, any and all connected devices and software should be positioned as a valuable tool designed to help them – not as a monitoring tool designed to spy on them. The same recommendation applies to healthcare workers. ApiJect Phase 2 may provide incentives to healthcare workers and clinics for achievements in

The global casino industry uses RFID technology to process trillions of dollars of casino chips each year

Low-power RFID chips, planned for integration with ApiJect in 2021, are already a widely used instant-tracking consumer-facing technology.

One of the most high-profile examples is the casino (gaming) industry, where 30+ million casino gaming chips worldwide are embedded with invisible RFID tags, each with a unique number that identifies the chip and its value. RFID tags made or licensed by Walker Tracking Systems process trillions of dollars in chip movements, typically in real time.¹⁰⁴ After ten years of 99.999% accuracy, RFID has revolutionized data collection and management for the gaming industry worldwide.

Walker Digital Tracking Systems will also develop a new, curved RFID tag that will be affixed to glass vials of medicine or vaccine, positioned under the label. This RFID tag will enable geo-location tracking of each vial, plus tracking of individual injections at the point of use. For the first time, pharmaceutical companies, national health ministries and global vaccination bodies will have a total tracking system for shipping and administration of glass vials and their contents.



providing care, such as recognition within the system and free phone minutes.

Summary:

When the mobile-connected, prefilled soft syringe and its data communication system are deployed at scale, nearly everyone in the world will be able to see where we have coverage and where we need to do better.

The time is growing near when every injection will be

documented and tracked, globally, to provide the vital intelligence that enables course corrections in the field, and continual adjustments for better planning. Put simply, the Internet of Things is coming to the world of safe injections and the benefits are numerous.

We believe that ApiJect’s affordable and practical new device and technology offers a leapfrog solution over the many challenges and costs associated with old-style glass vials and syringes and their administration.

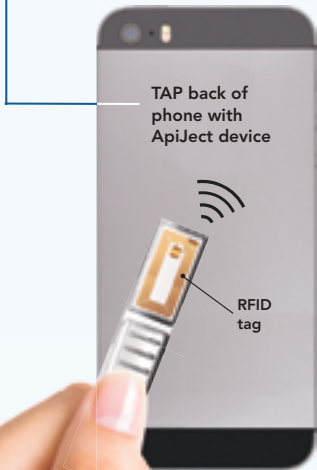
Infographic E

With ApiJect Phase 2, simply “tap and press” to use. Data is automatically captured, then uploaded and reported.

TAP

The health worker **TAPS** the **back** of their phone to the ApiJect device.

One tap uploads the ApiJect serial number to the cloud with time and geo-location (GPS) of activation.




TAP back of phone with ApiJect device

RFID tag

The serial number is associated with the drug name & dose; batch # and history; medic ID#; and other factors.


PRESS

The health worker **PRESSES** the bubble to inject the vaccine.



REPORT

Data is used to automatically generate useful **REPORTS** for anyone who needs them.*



Polio vaccinations in Kenya by date

Region 7 vaccine injections by clinic this week

Hep-B inoculations by city/town, daily/weekly/monthly

Injections by health worker in a specific clinic/time frame

* No patient-identifiable data included.

SECTION 8

Supplemental Information, Including Where to Learn More About ApiJect.



**Quick overview of ApiJect, the 2nd-generation compact Prefilled Auto-Disable Device (cPAD).
Marc Koska and Jay Walker: short biographies**

2nd Generation cPAD

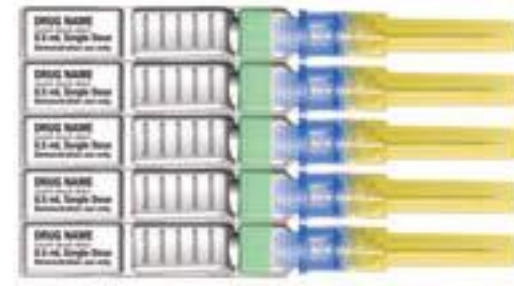
ApiJect: The first BFS cPAD – The “Soft” Syringe

PRODUCT SUMMARY

ApiJect devices can expand global coverage and equity of vaccine distribution while enhancing safety for patients and healthcare workers (1) below the current per-dose delivery cost of a multi-dose vial; (2) manufacturable by any pharmaceutical company; and (3) in a single-dose, non-refillable presentation. ApiJect is a single-dose compact Prefilled Auto-Disable device (cPAD) that uses well-established Blow-Fill-Seal (BFS) technologies to achieve new benchmarks in cost and safety.

THE APIJECT DEVICE

The ApiJect device is a cPAD created using BFS plastic technology (BFS cPAD). It is manufactured, filled, and sealed in a single aseptic process, contributing to a lower cost per dose delivered than a 10-dose vial presentation.¹ ApiJect devices are packaged singly or in strips of 5 or more contained in a blister pack with the biological, container, and Needle Hub preassembled. ApiJect can be manufactured from 0.1 to 2.0 mL doses with ID, SC, or IM needle lengths.



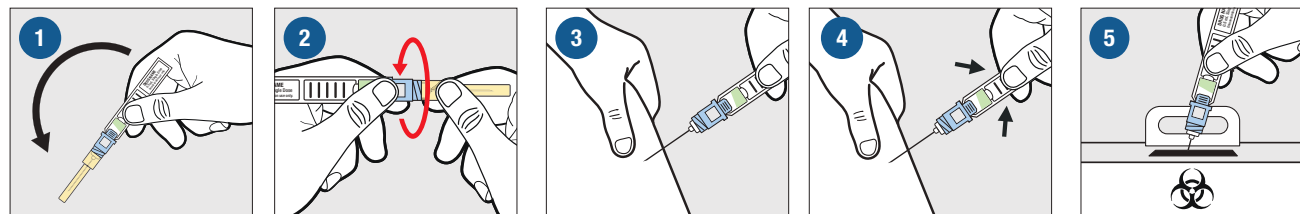
BLOW-FILL-SEAL (BFS)

BFS is an established manufacturing process in the healthcare field. More than 50 billion plastic units are produced for sterile medical contents every year.² A BFS machine creates the medical-grade LDPE polyethylene container, fills it with the biological, and seals it in a seamless aseptic process. Current BFS machines produce 30,000 injectable sterile doses per hour, enabling monthly BFS production of 21 million doses per month per machine.³ BFS ampoules are currently approved by regulators for use with GSK’s Rotavirus oral vaccine.

RATIONALE

- **Single dose:** Significantly reduces wastage, guarantees accuracy, facilitates outreach.
- **Prefilled:** Ensures correct dosage, and simplifies the injection process.
- **Non-refillable/single-use:** Eliminates patient-to-patient transmission of bloodborne pathogens.
- **Affordability:** Delivers total cost at or below price per dose of a 10-dose vial and syringes.
- **Simplicity:** Any healthcare worker can quickly vaccinate a patient with minimal training. Allows for patient self-injection when appropriate and regulator-approved.
- **Compact:** Enables easy transport to remote areas and efficiently utilizes the cold chain.
- **Lightweight:** Significantly less weight compared to single- or multi-dose glass vials and plastic syringes.⁴
- **Flexible Design:** Meets specific needs for different markets and contents by enabling custom tailoring of the container.
- **Environmental:** Significant reduction in energy and raw materials to manufacture. Easier to recycle and dispose of.⁵
- **Manufacturing Speed:** Shorter lead time to initiate high-volume production.

INSTRUCTIONS FOR USE (after health worker washes hands & cleans patient injection area)



1 SHAKE DOWNWARD
Flick device to move drug into the liquid chamber.

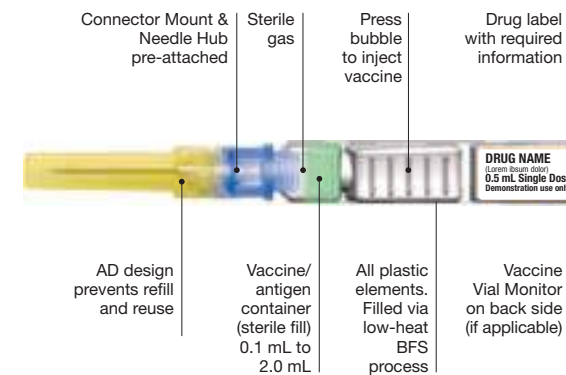
2 ACTIVATE
Activate by holding the blue hub and twisting the yellow cap at least 360°.

3 UNCAP AND INSERT
Remove the needle cap. Keep needle tilted downwards. Insert when ready.

4 SQUEEZE
Press and hold air chamber (closest to the label), until all of the liquid is in the patient. Takes about 5 seconds.

5 DISPOSE
Do not re-cap the needle. Discard the used prefilled syringe in a puncture-proof safety disposal bin.

NEEDLE HUB + BFS CONTAINER



MANUFACTURING PARTNERSHIPS & ADVISORS

ApiJect is supported by a team of internationally-approved manufacturing partners:

- Rommelag (Switzerland) – The inventor of and world leader in BFS technology.
- Tae-Chang Industrial (South Korea) – A leading needle and syringe manufacturer.
- HMD Healthcare (India) – One of the world’s five largest medical device suppliers.

ApiJect receives support and advice from established innovation-support organizations, including: The Bill and Melinda Gates Foundation and PATH.

Production

With assistance from ApiJect’s partners, several facilities around the world will be ready to produce ApiJect units in late 2020 pending regulatory approval. Each will have fully automated, high-volume production lines capable of producing 21 million doses per month per BFS machine. Pharmaceutical companies that choose to offer their product in ApiJect have the option of purchasing BFS machines and installing ApiJect production finishing lines in their facilities.

Regulatory

ApiJect’s Needle Hub and BFS container will undergo separate regulatory submissions followed by an application for a combination registration in the EU and the U.S.

Optional Configurations

The purchaser may order ApiJect in a variety of configurations based on preference:

- Single-item or 5 or more dose strip packaging
- ID, SC, or IM needle sizes
- Custom BFS container shapes and colors

Uses

ApiJect can be used for any type of injection, including vaccines, pharmacologicals, contraceptives, hormones, and emergency

field campaigns. Improved epidemic response and disaster preparedness are also possible as each BFS machine can mass-produce 21 million doses a month with lead times of a few weeks. Glass vial lead times are eliminated.

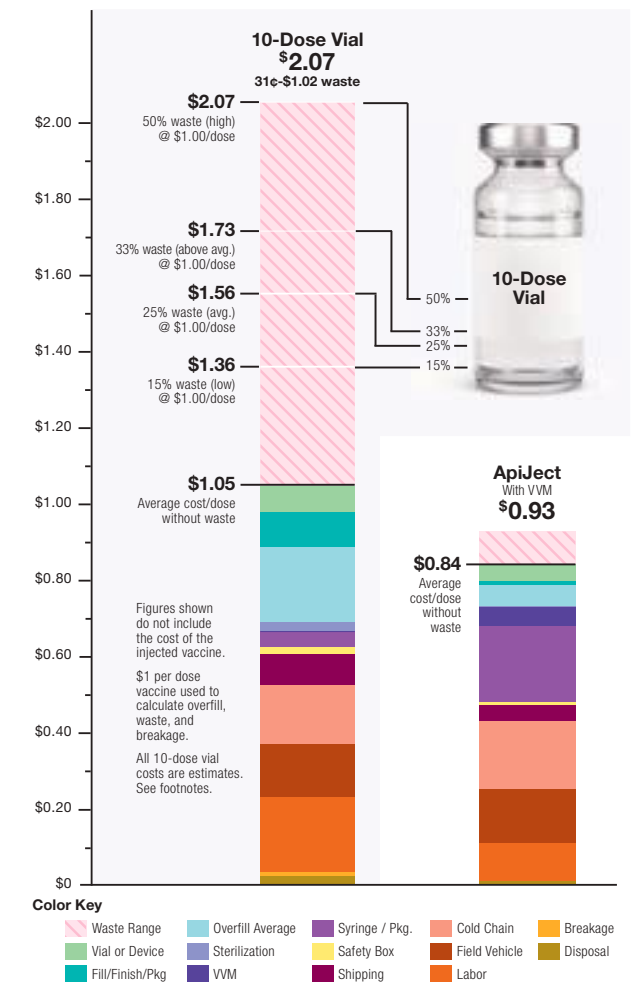
Cost

The ApiJect device can be manufactured and delivered at a lower cost per dose than multi-dose vials. ApiJect has committed to a Global Access price below the total cost of the same contents delivered in a 10-dose vial format.

History of the ApiJect Device

Supported by the Bill & Melinda Gates Foundation in association with PATH, Marc Koska, the inventor of the K1 Auto-Disable Syringe, has designed a Needle Hub that can be affixed to a BFS container to create a prefilled “soft” syringe. The ApiJect team has worked closely with Rommelag, HMD, and T-C Industrial to create a market-ready product and global manufacturing system pending regulatory approval.

COMPARING APIJECT TO 10-DOSE VIAL COST⁶



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To Learn More About ApiJect, Download Our White Papers

Downloads are available at apiject.com/publications



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



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



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



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



The Marc Koska Story

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- In addition, we assume that at least 66 million syringes will be needed for mixing vaccine with adjuvant and a minimum of 660 million syringes will be needed for injection of vaccine. We also assume that some of the syringes distributed for injecting seasonal flu vaccine may also be available for use, but this number will depend on timing of availability of pandemic vaccine.
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THE TEAM BEHIND APIJECT: Marc Koska and Jay Walker

MARC KOSKA, OBE, SOCIAL ENTREPRENEUR

The inventor of ApiJect, the first BFS cPAD device, is Marc Koska, one of the world's most respected and successful social entrepreneurs.

In the mid-1980s, Mr. Koska invented the K1 Auto-Disable Syringe, a device that stops the spread of blood-borne disease and infection by making it impossible to reuse medical needles and syringes. In 2005 he founded the nonprofit SafePoint Trust to educate children about the danger of employing used needles. To date Marc's invention and leadership are estimated to have saved 10 million lives. In 2015, WHO Director Dr. Margaret Chan announced a new global policy on injection safety, promoting auto-disable syringes. The K1 is now licensed by 14 global manufacturers. Among many other honors bestowed on Mr. Koska, he was made an Officer of the Order of the British Empire for his "contribution to global healthcare."

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JAY WALKER, INVENTOR, ENTREPRENEUR

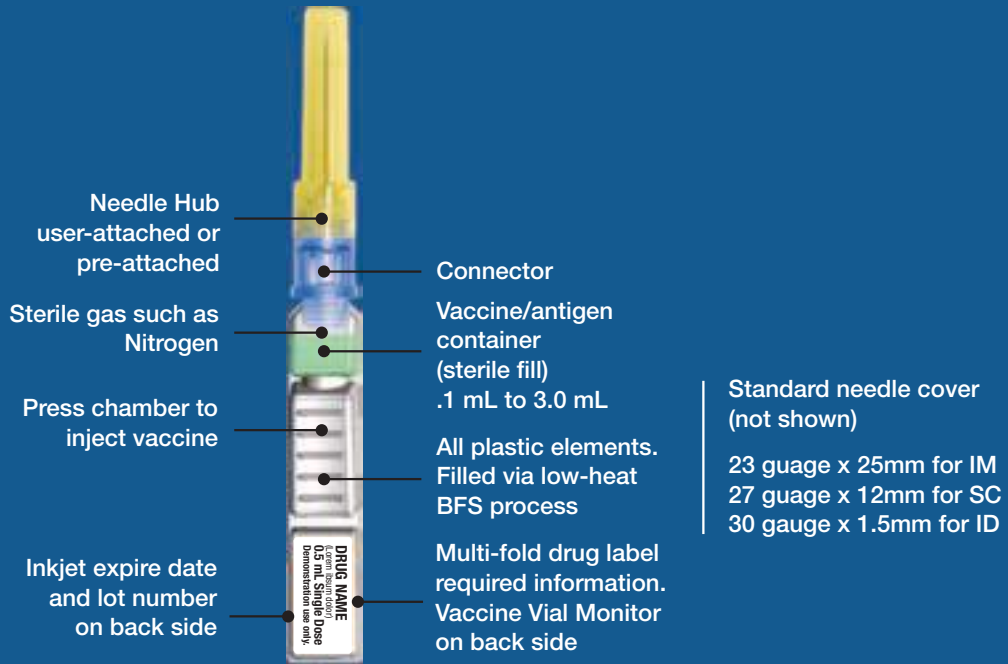
Jay Walker leads ApiJect's technology efforts as well as its business and commercialization activities. He is best known as the Founder of Priceline and Curator of TEDMED.

A serial entrepreneur, Mr. Walker has founded three companies that have gone from launch to 50 million customers each. Mr. Walker is the world's 10th most patented living inventor, with more than 750 issued U.S. patents in technology-related fields. Active in the field of medicine since 2012, Mr. Walker serves as Chairman and Curator of TEDMED, the health and medicine edition of the world-famous TED conference. He is also Chairman of Upside, a travel and technology company that serves the unmanaged business traveler. A passionate student and practitioner of imagination, Mr. Walker founded and curates the Library of the History of Human Imagination, which *Wired* magazine called "the most amazing private library in the world."

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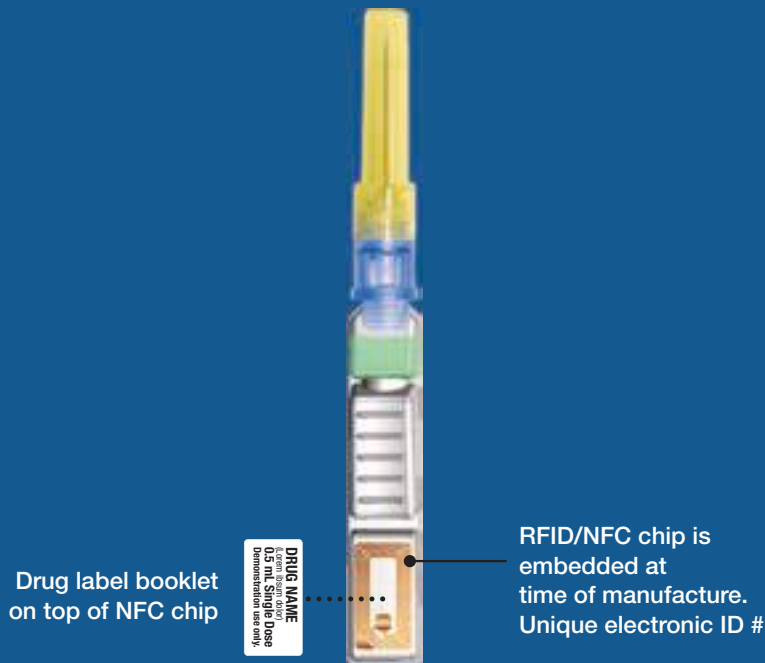
Phase 1 – BFS Container + Needle Hub

User-attached or factory pre-attached (actual size)



Phase 2 – BFS Container + Needle Hub + RFID / IoT

User-attached or factory pre-attached (actual size)





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Any forward-looking statement speaks only as of the date on which such statement is made and the Company undertakes no obligation to correct or update any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by applicable law.

Risk Factors

We have a limited operating history, and have not produced a profit. We were formed recently and have a limited operating history, and have incurred losses since our inception. We expect to continue to incur significant sales and marketing, research and development, regulatory and other expenses as we expand our operations. The losses we incur may fluctuate significantly from period to period. We will need to generate significant additional revenue in order to achieve and sustain profitability. Even if we achieve profitability, we cannot be sure that we will remain profitable for any substantial period of time.

Our technology was developed in the context of vaccination prior to the outbreak of the COVID-19 pandemic, and while we believe it will be effective in delivering a vaccine for COVID-19, there is no guarantee our technology will be effective in doing so. Our technology was originally formulated for delivery of vaccines throughout the developing

(continued on back)

world. It was not created for delivery of COVID-19 to a worldwide community. While we believe that our technology has applications for COVID-19 vaccine delivery, until such time as a vaccine is actually available and it can be tested with our product, there is no guarantee that our technology can actually be used to effectively deliver a COVID-19 vaccine.

Our technology can be deployed to fight COVID-19 only to the extent that a vaccine is created, and we are not currently working on creating or developing such a vaccine. To the extent that traditional vaccine manufacturers are unable to develop and obtain approval for a vaccine, we may not be able to deploy this technology to fight COVID-19. Our business plan is dependent upon the creation of a vaccine for COVID-19. We are not engaged in, nor do we intend to engage in, the development of such a vaccine. While we understand that a number of third parties are in the process of developing such a vaccine, there can be no guarantee that they will be successful, and if they are unable to do so, we may not be able to pursue our current business plan.

We have limited experience in commercializing our technology for mass production, and we may be unable to commercialize our technology in a timely fashion in order to respond to the COVID-19 pandemic, or at all. Our business plan includes a mass production of COVID-19 vaccinations. To date, our business model has been built around developing technologies for the delivery of vaccines in the developing world, and therefore we do not have any experience in commercializing our technology for mass production of over a billion units. As a result, even if manufacturers are able to develop a vaccine, there can be no guarantee that we will be able to commercialize our technology in time to meet their needs for distribution, or at all.

Our business plan is dependent upon our government contract with the U.S. federal government, and there can be no assurance that the U.S. federal government will continue to support the programs underlying our government contract. We are party to a government contract with the U.S. federal government to use our technology for delivery of COVID-19 vaccines. Our business plan is substantially dependent upon that contract, and as such, any changes in U.S. federal government policy relating to the programs that underlie our contract may adversely affect our business.

Our business plan includes the commercialization of a COVID-19 vaccine for distribution outside of the United States; to the extent that our intellectual property rights in our technology are inadequate to protect us from competition—either in the United States or elsewhere—we may be unsuccessful in deploying our business plan. Our technology is protected by certain patents and trade secrets. The validity of those patents and trade secrets may be challenged. Further, we intend to distribute our technology throughout the world; to the extent that our intellectual property is not recognized—or other jurisdictions do not have adequate means to protect the exclusivity of our intellectual property—we may be unsuccessful in preventing the unauthorized deployment of the technology by third parties either in the United States or elsewhere.

Our business plan depends on the construction of facilities to manufacture our technology, and we may be unable to complete our capital expenditure plan on the current timeline or at all. We have not yet begun production of the thirty facilities needed to manufacture our technology in order to respond to the COVID-19 pandemic. Although we expect to use the proceeds of the offering to fund the construction and commercialization of those facilities on a timeline that is expected to meet the availability of vaccines, there can be no guarantee that construction and commercialization will occur on our current timeline, or at all.

We are a public benefit corporation organized under Delaware law, and we are not obligated to maximize shareholder profit. We are organized as a public benefit corporation under Delaware law. Public benefit corporations are a relatively new class of corporations that are intended to produce a public benefit and to operate in a responsible and sustainable manner. Under Delaware law, public benefit corporations are required to identify in their certificate of incorporation the public benefit or benefits they will promote and their directors have a duty to manage the affairs of the corporation in a manner that balances the pecuniary interests of the stockholders, the best interests of those materially affected by the corporation's conduct, and the specific public benefit or public benefits identified in the public benefit corporation's certificate of incorporation. Public benefit corporations organized in Delaware are also required to assess their benefit performance internally and to disclose publicly at least biennially a report detailing their success in meeting their benefit objectives.

As a public benefit corporation, since we do not have a fiduciary duty solely to our stockholders, we may take actions that we believe will benefit our students and the surrounding communities, even if those actions do not maximize our short- or medium-term financial results. While we believe that this designation and obligation will benefit the Company given the importance to our long-term success of our commitment to helping the United States respond to, and/or prepare for, a public health emergency or other critical event, it could cause our board of directors to make decisions and take actions not in keeping with the short-term or more narrow interests of our stockholders. Any longer-term benefits may not materialize within the timeframe we expect or at all and may have an immediate negative effect.

In addition, there is no assurance that the expected positive impact from being a public benefit corporation will be realized. Accordingly, being a public benefit corporation and complying with our related obligations could negatively impact our ability to provide the highest possible return to our stockholders.