OCTOBER 2021

ApiLabs Red Reports:

A set of reports on eliminating unsafe injections globally…and related issues.

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When Injections Spread Disease

Worldwide use of contaminated vials and syringes in clinical settings leads to 1.3 million deaths per year…and spreads disease to millions.[1]

"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."[2]

DR. BENEDETTA ALLEGRANZI
COORDINATOR
WHO INFECTION PREVENTION AND GLOBAL CONTROL UNIT

Improper use of syringes and multi-dose vials often leads to contamination of equipment, which spreads disease.

Tragically, a technology designed to save lives often costs lives when used improperly.

For 165 years the global medical establishment has relied upon the same basic technology for injections. Small glass vials of medicines or vaccines are distributed to points of care around the world. From these vials, syringes are carefully filled, calibrated for the correct dose, and then injected and discarded.

In high-income countries, single-dose vials are used. The vial contains just enough vaccine or medicine for a single injection. After the injection, the vial is discarded along with the syringe, so patients can always trust that they get a safe injection. In the rest of the world, health ministries and organizations use multi-dose vials because it's more economical to buy medicine and vaccine, like everything else, in larger containers. Lower cost is why the 10-dose glass vial accounts for between 75% to 80% of global volume of injectable vaccines. In some areas, the rate is 90%.[3]

Over the decades, traditional syringes and 10-dose vials have saved countless lives – but they also cost many lives through cross-contamination and infection in clinical settings. This is a global problem. It occurs in both high-income and low-income countries.

In some low-resource settings, syringes are reused over and over. When a contaminated syringe is filled from a vial, it contaminates the vial's contents and invisibly spreads diseases such as HIV and hepatitis.[4]

As recently as 2016, up to 70% of injections were still given with reused vials and syringes in some countries.[7]

In some settings, the improper reuse of syringes still occurs at an alarming rate.

It has been 18 years since WHO estimated that cross-contamination from reused vials and syringes resulted in 1.3 million early deaths per year. During the intervening years, WHO and UNICEF have implemented their policy requiring that all vaccines must be purchased in the Auto-Disable syringe format.

Yet according to Dr. Benedetta Allegranzi, coordinator of the WHO Infection Prevention and Global Control Unit, "achievements were not equal in different parts of the world. While much progress has been made in immunization, the safety of therapeutic injections remains a challenge."[5]

Table[6]

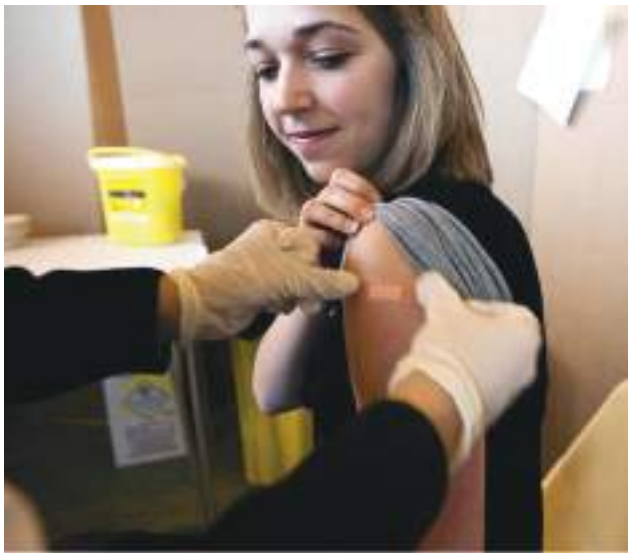
Disease or infection	Est. % of new cases caused by unsafe injections	Est. # of patients infected per year
Bacterial	7%	3 million
Hepatitis B	25%	15 million
Hepatitis C	8%	1 million
HIV	14%	340,000+
Top 20 Total	5-10% est.	10's of millions

In 2016, Dr. Allegranzi reiterated that "up to 70% of injections…are given with reused syringes and needles in some developing countries."

In fact, WHO estimates that in the year 2000, some 6.6 billion injections were given with reused equipment. That represents 39.6% of the 16 billon total injections of medicine and vaccine that WHO believes are administered each year in the developing world.

The danger of unsafe injections is classified by medical professionals with other medically-caused injuries, along with – for example – hospital acquired infections or giving patients the wrong treatment due to a mistaken diagnosis. These medically-caused injuries are common enough to have been given a collective label: the medical world refers to them as "iatrogenic" harm.

Cross-contamination during injections also occurs in high-income countries.



The problem of contaminated vials & syringes is not confined to low-income countries.

High-income countries also experience significant numbers of infections from cross-contamination when established protocols are not followed by clinical staff.

The CDC has documented dozens of U.S. outbreaks of hepatitis in the last decade.[8] Experts believe many of these outbreaks were caused by clinical reuse of contaminated syringes.

A 2010 survey of more than 5,000 U.S. nurses revealed "an alarming lapse in basic infection-control practices associated with the use of syringes, needles, multiple-dose vials, single-use vials, and flush solutions… clearly placed patients at risk for transmission of blood-borne diseases, according to information sent to the Institute for Safe Medication Practices (ISMP)."[9]

According to the survey, "Fifteen percent of respondents reported using the same syringe to re-enter a multiple-dose vial numerous times. Of this group, about 7% reported saving those multiple-dose vials for use with other patients."[10] The result is headlines like this one from *The American Journal of Infection Control* in 2013: "Hepatitis C transmission due to contamination of multi-dose medication vials: summary of an outbreak and a call to action."[11]

Or this headline from the *Morbidity Mortal Weekly Report* in 2012: "Multiple outbreaks of hepatitis B virus infection related to assisted monitoring of blood glucose among residents of assisted living facilities – Virginia, 2009-2011."[12]

Cross-contamination of vials and syringes has significantly contributed to the spread of pandemics such as Ebola.

When an entire population requires emergency vaccination, the risk of spreading disease is even greater.

In epidemics and pandemics, contaminated vials and reused syringes can be disastrous.

As researchers reported in *The Pediatric Infectious Disease Journal,* "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."[13]

Ebola is the subject of many mistaken beliefs, including widespread misunderstanding of how it actually spreads. While Ebola is not transmitted through airborne dispersal like a flu, it does have mechanisms and transmission routes that extend beyond direct contact with the bodily fluids of an infected person or direct contact with the remains of an Ebola victim.

One of the most insidious of these additional transmission routes is contaminated syringes and vials. In a national emergency where authorities are arranging for mass vaccinations, syringes and vials can become infected through reuse and cross-contamination.

These in turn can be caused by hurried administration or improper technique, motivated in some low-resource settings by a desire to make maximum use of limited supplies. The motive may be understandable, but the results can be deadly.

Reusing a syringe once can contaminate a vial's contents, infecting all patients injected after.

Giving injections to people who carry a blood-borne disease guarantees that syringes will become contaminated with that disease.

How do syringes and 10-dose vials get contaminated in the first place? The short answer is improper reuse of syringes. That is the reason why WHO has long mandated the use of Auto-Disable syringes for vaccines.

But in low-resource countries, the 10-dose vial remains the most popular format due to its low cost.[21]

In order to promote safe use of this format, WHO has issued strict guidelines covering its use. These guidelines include discarding each syringe after a single use. The administrator of a vaccine is supposed to use a fresh, sterile syringe to withdraw each vaccine dose from the 10-dose vial and inject the next patient. Unfortunately, in many clinical settings, these guidelines are not followed. Improper reuse of equipment creates two possible routes for contamination: contaminated syringes and contaminated vials.

> "Injections from contaminated vials, caused by employing re-used syringes and improperly sterilized needles, played a major role in some areas of the early Ebola outbreaks."[14]

A clean, sterile syringe typically becomes contaminated

Disease spreads from one patient to several patients through a contaminated syringe in a simple, yet insidious process.

Syringes become contaminated in the ordinary course of giving injections to patients who are already infected.

Typically, a 10-step process occurs:

1. The health worker uses a fresh, sterile syringe to withdraw a dose of vaccine from a 10-dose vial.
2. The health worker uses that syringe to inject the vaccine into a patient who is carrying a disease.
3. When the health worker retracts the needle from the infected patient, microscopic droplets of the patient's infected blood are suctioned out of the patient, into the needle.

4. These infected blood droplets travel through the needle into the barrel of the syringe.
5. The syringe is now contaminated, even though the amount of infected blood may be so tiny as to be invisible.
6. In some clinics, healthcare workers routinely disregard protocols and fail to dispose of used syringes. Instead, they reuse them. The health worker may attempt to sterilize the syringe by washing it in alcohol or boiling it in water or alcohol. However, the infected blood remains and the disease's pathogens remain active.
7. When the next patient needs an injection, the health worker uses the infected syringe to withdraw a fresh dose from a vial. Even if a brand-new vial is opened,

when an infected patient receives an injection.

the vaccine drawn into the syringe will become contaminated when it makes contact with the microscopic blood droplets in the barrel of the syringe.

8. When the contaminated syringe is used to inject the new patient with the vaccine, the patient also receives some of the pathogen from the previous patient's blood. The infection has now been spread by the clinic. (Contaminated syringes are the first route for contamination. The second route is described below; see step 10.)

9. Once the needle of the contaminated syringe is inserted into the vial, all the contents of that vial becomes contaminated.

10. As a result, all subsequent doses withdrawn from that same contaminated vial can spread infection to additional patients. This remains a danger even if a fresh, sterile syringe is used each time for these subsequent injections. (Contaminated vials are the second route for contamination and the spread of disease.)

The first five steps in this process do not automatically result in unsafe injections but they do open the door to potential contamination and the spread of disease.

The critical steps that degrade a safe procedure into a dangerous, high-risk activity are Step 6 (attempting to sterilize a contaminated syringe), Step 7 (refilling a used syringe) and Step 8 (injecting a patient with a used syringe).

There are many reasons why reuse of syringes persists – including cost, procurement and regulatory issues.

So long as reusable syringes are provided, some health workers will continue reusing them.

Given that Auto-Disable syringes have become the global standard for vaccines, and have become more affordable in recent years, it may seem puzzling that reusable syringes continue to be used for most of the other 90% of medical injections, which are therapeutic injections. There are several reasons for this, including:

1. Cost factors: Prefilled Auto-Disable devices such as Uniject™ have become price-competitive with single-dose vials, but they remain more expensive than 10-dose vials and do not scale to large quantities.
2. Procurement practice: According to WHO's Dr. Allegranzi, in some countries, syringes are not procured in the same market chain as injectable medicines, and the responsible health ministries may not know about injection safety needs.[15]
3. Regulatory environment: Syringes are not well regulated in certain nations. Consequently, their markets are often "flooded with substandard product."[16]
4. Unqualified or poorly trained health workers: Healthcare workers in some countries have "ingrained" habits of reusing syringes, said Dr. Allegranzi.[17] And, in some regions, unqualified individuals falsely calling themselves "injection doctors" travel among rural populations, giving injections to unschooled patients who don't know any better. Waste scavenging and repackaging of used syringes remains an issue in some countries as well.[18]

Recent headlines in the news demonstrate that contaminated syringes remain a deadly problem.

No matter how strict the protocols, they will inevitably be broken at times.

Contaminated Measles Vaccine Kills 15 Kids in South Sudan (Jun.02.2017)

JUBA, South Sudan – Fifteen young children have died in a botched measles vaccination campaign…The United Nations said the children died of "severe sepsis/toxicity" from the contaminated vaccine... One syringe was used for all the children during the four-day campaign, and the vaccine was stored without refrigeration the entire time.

Fake doctor in India infects villagers with HIV by using tainted syringes (AP February 6, 2018)

LUCKNOW, India – A fake doctor treating poor villagers in northern India for colds, coughs and diarrhea has infected at least 21 of them with HIV by using contaminated syringes and needles, a health official said Tuesday.

Patients being tested for HIV after nurse reused syringes (Jun.12.2018)

TAHLEQUAH, Okla. – A Cherokee Nation hospital in Oklahoma is testing more than 180 patients for HIV and hepatitis after allegations that a nurse reused syringes to administer medications. The nurse violated protocols by using the same vial of medication and syringe to inject multiple intravenous bags at W.W. Hastings Hospital in Tahlequah, according to Cherokee officials.[19]

ApiJect's Prefilled Injector* is designed to deliver only one dose. There is no vial to cross-contaminate.

Injections with low contamination risk can also be economical.

Can the global health community prevent the spread of blood-borne disease through improper injections? Yes – with innovative injector design and manufacturing. ApiJect is a new, prefilled delivery system* that is designed to prevent any reuse of contaminated syringes. In addition, ApiJect eliminates any possibility of cross-contaminating the contents of a vial, because it does not use vials.

The ApiJect Prefilled Injector* will consist of three parts: (1) a prefilled plastic container; (2) a Connector; and (3) an attachable Needle Hub with a hypodermic needle and safety cap. The three parts will ship separately, ready for push-to-assemble activation.. Once assembled, the needle cannot be detached or reused. Since ApiJect is prefilled, there is no need to withdraw liquid from a vial.

With no vial, there is no possibility of vial contamination. (Safety is also enhanced because prefilling each ApiJect syringe at the time of manufacturing reduces over- and under-dosing risks.) Finally, once a patient is injected, the ApiJect Container would be very difficult to refill or reuse.

With ApiJect, safety also supports increased economic efficiency. ApiJect believes its Prefilled Injector will cost less per dose upfront and will also cost up to 50% less per dose delivered, depending on wastage factors. This could enable national health ministries and international health organizations to stretch their budgets farther, moving closer to full coverage and equity, while reducing contamination risk. By reducing or eliminating contamination of injection equipment, the planned ApiJect Prefilled Injector could save more than one million lives around the world every year.

* Products shown for informational purposes only, not for use in product promotion.
ApiJect's Prefilled Injector and other products have not been reviewed or cleared by FDA or other regulatory authorities for distribution.

It is a tragic irony that although multi-dose glass vials and syringes have saved countless millions of lives, they are also responsible for more than 1 million deaths per year through cross-contamination and the spread of infection in clinical settings.

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“Infection prevention and control is the backbone of good hygiene and all its preventive power.” [20]

DR. MARGARET CHAN
FORMER DIRECTOR-GENERAL, WHO

Billions of Glass Vials Every Year With Unintended Consequences

A 165-year-old technology, multi-dose glass vials and syringes that are too often reused, won't get us to the level of coverage, equity and safety that the world needs today. It's time to rethink the underlying system.

Contaminated syringes cause
1.3 million deaths every year.
By replacing glass vials and
syringes, a 165-year-old technology,
with a more efficient drug delivery
system, the world can achieve
greater coverage, equity, and safety.

Most of the world buys vaccines and medicines in glass vials which have the lowest manufacturing cost of all major formats.

But manufacturing is only part of the total cost per dose delivered. Many hidden costs make glass more expensive than it first appears.

Excluding vaccine cost (and not counting waste), the cost for transportation and cold chain storage is the greatest contributor to the Total Cost of Delivery for vaccines.[1] Glass is expensive to produce as it is very energy-intensive, and it is heavy to transport, particularly to the kinds of remote locations most in need of vaccines and medicines. However, the pharmaceutical industry is reluctant to make changes to its packaging formats due to the cost of switching.

Beyond the obvious costs of production and transport, glass vials come with numerous additional hidden costs. These include breakage and delamination (flaking), which can affect product safety and efficacy. Vaccines in multi-dose vials require high levels overfill and incur high wastage without preservatives. Appropriate disposal is costly in low-resource settings; and the cost per dose of manufacturing for single-dose vials is high compared to multi-dose vials.[2]

Only medical professionals can give injections from glass vials.

Vaccines and most medical injections must be given by trained practitioners, but in much of the world, not enough trained medical staff are available. Millions of patients don't get the medical injections they need.

It is estimated that approximately 7.2 million health workers are needed to provide essential health services worldwide.[3] That need is met by doctors and nurses, and also community health workers (CHWs). Even with an estimated 1.3 million CHWs,[4] there is a shortage of healthcare workers in the world because of emigration, rural/urban maldistribution, and changes in population demography,[5] resulting in a shortage that is increasingly acute in developing countries and rural areas of the world.[6]

This shortage of health professionals who can give injections leaves communities vulnerable to death and disease. But, as Dr. Henry Perry, senior scientist at Johns Hopkins Bloomberg School of Public Health, stated, "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."[7]

Vials make it easy to sell counterfeit medicine.

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

The World Health Organization (WHO) estimates that 10% of the global market for pharmaceuticals is comprised of counterfeits; the percentage of phony products can be as high as 50-70% in developing countries according to some.[8] The contents of glass vials can't always be trusted.

Drugs counterfeited included antibiotics, hormones, analgesics, steroids, and antihistamines, and can be grouped into six categories: (1) Products without active ingredients, 32.1%; (2) Products with incorrect quantities of active ingredients, 20.2%; (3) Products with wrong ingredients, 21.4%, (4) Products with correct quantities of active ingredients but with fake packaging, 15.6%; (5) Copies of an original product, 1%; and (6) Products with high levels of impurities and contaminants, 8.5%.[9] Counterfeit drugs result in an annual death toll of approximately 1 million, according to the WHO.[10]

With small vials, it is 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.

Glass vials require precision in selecting the right vial with the right drug or vaccine to fill the syringe. A lack of precision in this critical step can cost people their lives.

Unfortunately, in busy clinics with few health workers and many patients, it is far too easy to make mistakes when utilizing glass vials and syringes for injections. This can result in incorrect medicine being injected, inaccurate doses, and needlesticks.

According to an advisory from the U.S. Department of Health and Human Services' Patient Safety Network (most recently updated in September of 2019), "A review of 36 studies on caregiver medication errors found error rates ranging from 2%–33%, with dosage errors, omissions, and wrong medication the most common types of administration errors."[32]

Hand-filling syringes makes it easy to give patients the wrong dose.

Healthcare professionals must withdraw precisely the right amount of vaccine or medicine from a multi-dose vial. This requires knowledge and skill. It's easy to under-dose or over-dose a patient, especially in busy, understaffed clinics and hospitals.

Glass vials and syringes require a trained healthcare professional to administer injections. This includes skillfully withdrawing precisely the correct amount of medication or vaccine from the vial to fill the syringe for each injection.

Without this skill and training, patients are vulnerable to receiving the wrong amounts of medicine or vaccines.

Contaminated vials and/or reusable syringes can be deadly.

UNICEF buys only Auto-Disable syringes for vaccines. Other buyers may get reusable syringes that cannot be re-sterilized, leading to mass infections (20 million+ casualties per year from death, injury, and illness).

Up to 70% of injections are given with reused syringes and needles in the developing world,[11] and unsafe injections result in 15 million Hepatitis B infections (25% of new cases), 1 million Hepatitis C infections (8% of new cases), and 340,000 HIV/AIDS infections (5 – 14% of new cases).[12] A 2010 survey of 5,446 health care professionals revealed how these infections can happen:[13]

- Nearly 1% of respondents acknowledged that they sometimes or always reused a syringe for more than one patient after changing only the needle.
- 6% admitted to sometimes or always using single-dose or single-use vials for multiple patients.
- 15% of respondents reported using the same syringe to re-enter a multi-dose vial numerous times.

Internal glass flakes off and contaminates 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. Vials must be tested and retested to guard against this problem.

This problem is called delamination. When the flakes, often not visible to the human eye, mix with the vial contents, the result is dangerous contamination.

Flaking is common in glass vials and occurs when chemicals from the product or the manufacturing process cause the glass surface of the vial to delaminate or discolor.[14]

This can happen at any point during the vial's life: manufacturing, heat treatment, sterilization, or stability testing, making it especially difficult to identify, and especially dangerous.[15] Delamination poses a serious health risk to any patient who receives an injection of a contaminated drug product, reducing its safety and efficacy.

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.

Over the past five years, more than 20 product recalls have been associated with glass issues, and over 100 million units of drugs packaged in vials or syringes have been withdrawn from the market.[16]

In the 10 years prior, approximately two million glass vial and syringe units were recalled.[17] Additionally, nine warning letters citing glass-related problems were issued in the past five years, and seven during the decade before.[18]

When a glass vial breaks in transit, the entire pallet of vials filled with vaccine must be discarded. This can amount to nearly 1,000 vials lost.[33]

These limitations of glass packaging cost companies millions of dollars in lost revenue, but the industry is reluctant to adopt new technologies due to the cost of switching formats.

Short ID needles cannot be used with glass vials.

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). Short needles and a prefilled single-dose format eliminate the need to prepare vials and syringes.

Needles and syringes limit accessibility to needed medicines and vaccines by requiring a trained medical professional to administer them in clinical settings. But when using a prefilled single-dose format, intradermal injections – those just under the skin – require simple training for a healthcare worker to administer, and can even enable patients to self-inject, eliminating the need for a healthcare worker to administer a vaccine or medicine, as well as the need to prepare a needle and syringe.[19]

In a world where there is a shortage of healthcare workers, this is life-changing for millions of people, including an estimated 214 million women in developing countries who would like to delay or prevent pregnancy but are not using any method of contraception.[20] Replacing glass vials and syringes has the potential to transform the way people access and receive medicines and vaccines in low-resource, non-clinic settings.[21]

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.

Traditional glass vials and the accompanying syringes are labor-intensive. The exact amount of medicine needs to be measured and withdrawn from each vial, using a separate syringe to withdraw then inject the vaccine or medicine. A 2014 time and motion study conducted by PATH indicated that dispensing vaccine from a 10-dose vial takes exactly twice as long per injection as dispensing vaccine from a prefilled single-dose device. On average, it took healthcare workers 15.2 seconds to give an injection from a 10-dose vial and 7.6 seconds to give an injection from the prefilled device.[22]

In resource-challenged settings that are limited by a lack of healthcare professionals, needles and syringes take up valuable time. And mistakes can be deadly. If healthcare workers could inject patients in non-clinical settings and if patients had the ability to inject themselves because needles and syringes weren't necessary, it would increase coverage of people in need of life-saving medicines.

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.

When glass is manufactured, the combustion of natural gas and the decomposition of the raw materials that form glass during the melting process lead to the emission of CO2.[23]

Additionally, glass manufacturing causes water pollution, uses non-renewable raw materials, such as sand and minerals, and produces waste from the by-products of those necessary raw materials, as well as the glass itself. [24-25]

Furnaces used to melt raw materials into glass need to burn 24/7, using a great deal of energy at a consistent rate. Glass manufacturing is not the most environmentally friendly process, and imposes many limitations to product safety and efficacy as well.

High energy needs for glass are wasteful and costly.

Glass manufacturing 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).

The industrial sector, encompassing manufacturing, mining, agriculture, and construction, accounted for nearly a third of total U.S. energy use in 2012. Of those industries, manufacturing, which includes the glass industry, accounted for a little more than half of total industrial energy use. Glass manufacturing is one of the economy's most energy-intensive industries.[26]

The bulk of energy consumed in the glass manufacturing industry comes from natural gas combustion used to heat furnaces that melt raw materials and form glass (most furnaces are natural gas-fired, but there are a small number that are electrically powered). Many glass furnaces also use electric boosting or supplementary electric heating systems to increase throughput and quality.[27]

In a pandemic, pharma companies buy up limited supplies of glass vials, leading to shortages. Manufacturing lead-time for additional glass capacity is lengthy, creating slow crisis response.

Raw materials requirements and manufacturing processes mean that glass vials must be ordered up to 6 months or more in advance. Too slow for rapid response during sudden outbreaks.

After raw materials are melted and refined, glass is formed and then finished to create a final product. Specific manufacturing processes depend on the intended product, and can include annealing (slow cooling), tempering, coating, and polishing, all of which require additional energy.[28]

Due to the very complex and methodical process of manufacturing glass, the process is slow, and also requires costly transport, which results in long lead times for the end product. This is not ideal to service mass outbreaks or crisis situations.

Syringes are 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.

Healthcare workers are always at risk for needlesticks when handling syringes that accompany glass vials, both when using them on patients and when disposing of them. This risk is often greater in areas where the ratio of healthcare workers to population needs and disease burden is small.[29]

The risk of needlesticks and, therefore, possible infection, further demonstrate that unsafe injections are dangerous not only for recipients, but for those delivering the necessary medicine or vaccine.[30]

Professional-only syringe injections drive ongoing clinical visits.

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

In low-resource settings, there are very few healthcare facilities, and patients often have to travel long distances to reach clinics, making access to ongoing medicine and medical attention difficult.

This, coupled with a shortage of healthcare professionals, leaves many people simply unable to access life-saving health interventions, including injections of vaccines and medicine. It is critical that vaccines and medicine be available at the community level, outside of clinics in the form of either self-injectables (where permitted at the option of regulatory authorities) or injectables that are easily administered by local community health workers.[31]

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Glass vials for vaccines and medicines have a hidden waste factor that drives up real costs considerably. Vials are also vulnerable to deadly contamination. Eliminating these problems requires eliminating glass vials.

ApiLabs

Blow-Fill-Seal Prefilled Injectors Support Many Use Cases for Global Impact

An affordable, single-use prefilled injector* could open new opportunities for coverage, access and equity for billions of people around the world.

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Making single-dose injection formats available using Blow-Fill-Seal technology could support cost and time savings throughout health delivery systems and supply chains, while also supporting greater coverage and equity of access in the last mile.

Affordable single-dose injection formats could help vaccines and medicines make it to the last mile.

In environments where cost is the primary factor, glass vials are not an ideal choice. Manufacturing glass vials is expensive and their weight imposes higher transport costs.

Excluding vaccine cost (and not counting waste), the cost for transportation and cold chain storage for glass vials is the greatest contributor to the Total Cost of Delivery for vaccines.[1] Glass vials are heavy to transport, and susceptible to breakage and delamination (flaking) when traveling to the end user, which can affect product safety and efficacy.

In many remote locations most in need of vaccines and medicines, these interventions need to be carried by people or transported on bikes or other small vehicles, where weight and size are prohibitive factors. Replacing glass vials and syringes with a new, affordable, single-dose format* that is small-sized and light-weight could potentially the "last mile" health delivery system and supply chain, ensuring medicines and vaccines reach more people who need them.[2]

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Prefilled injectors could potentially support greater coverage and equity by enabling more patients to be served with existing budgets.

Compact, prefilled, single-dose BFS injectors can be efficient and scalable.

The ApiJect Prefilled Injector* is designed for high-quality, highly scalable production, potentially supporting widespread coverage and access, even at the same healthcare budgets. The device is planned to leverage the scale and efficiency of the Blow-Fill-Seal (BFS) filling process to create aseptically filled, single-dose Containers that become prefilled injectors when married with ApiJect's attachable Needle Hubs.* In addition, ApiJect's devices will be lightweight, for low shipping costs and low breakage risk during transit.

With ApiJect's device, health workers can potentially save time because there is no preparation of a new needle and syringe for each patient; no withdrawal from a vial; and no checking of proper dosage. Due to efficient use of labor, single-dose injection formats have been shown to require up to 50% less time to perform the injection than traditional vials and syringes.[3]

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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 (where permitted by law and approved by regulatory authorities), more women would potentially be able to control their reproductive choices.

Family planning is not only fundamental to the well-being and autonomy of women, but also to the health and development of communities.[4] And when women and adolescent girls have access to a variety of contraceptives, they are more likely to find and use a method that meets their needs and preferences.[5]

Self-injectable contraceptives have the potential to be that option as they are highly effective, safe, and private, as well as able to increase access and empower women to manage their reproductive health.[6] This is confirmed by the World Health Organization (WHO) supporting self-injection where women have access to training and support.[7]

Short SC and ID needles become possible with a prefilled single-dose format.

Longer needles are needed to withdraw liquid from glass vials, but they require Mantoux-style injections (often inaccurate) for shallow intradermal injections, important for some vaccines and medicines.

Needles and syringes limit accessibility to needed medicines and vaccines by requiring a trained medical professional to administer them in clinical settings. Intradermal injections – those into the skin – require simple training for a healthcare worker to administer, and can even enable patients to self-inject, eliminating the need for a healthcare worker to administer a vaccine or medicine, as well as the need to prepare a needle and syringe.[8]

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, a prefilled single-dose device can enable millions of community health workers to administer vaccines and medicine to millions of children, new mothers and adults.

It is estimated that approximately 7.2 million health workers are needed to provide essential health services worldwide.[9] That need is met not only by doctors and nurses, but community health workers (CHWs). Even with an estimated 1.3 million CHWs in the world,[10] there is a shortage of healthcare workers, leaving communities vulnerable to death and disease. If CHWs were empowered with tools adaptable to rural and fragile settings, they could help fill the gaps in access to care.

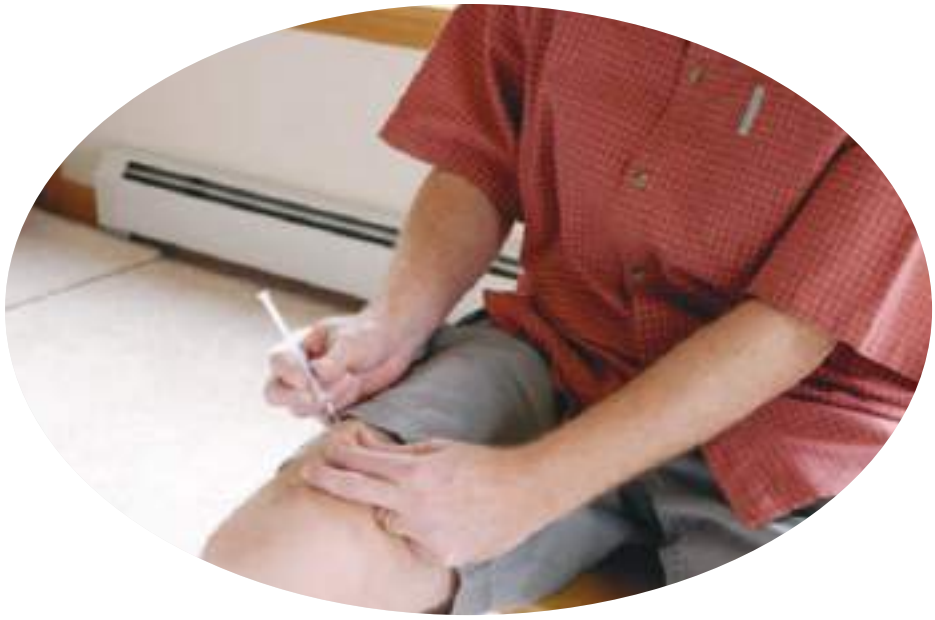
As Dr. Henry Perry, senior scientist at Johns Hopkins Bloomberg School of Public Health, stated, "If CHWs are used to deliver the interventions they are capable of delivering, and if 100% coverage could be attained, then the lives of 3.6 million children would be saved every year."[11]

Oxytocin and Hep-B at Childbirth

In the developing world, 60% of women give birth with no medical professional present. As a result, 800 mothers a day die from hemorrhage. Often the birth dose of Hep-B is not administered as well. A prefilled injector could be used to administer HepB and low-cost Oxytocin to save lives.

Poor women in remote areas are the least likely to receive adequate health care; this is especially true for regions with low numbers of skilled health workers. Other barriers to maternal health include poverty, distance, lack of information, inadequate services, and cultural practices. These obstacles result in millions of births each year unassisted by a midwife, a doctor, trained nurse, or other skilled health personnel.[12]

Almost all maternal deaths (99%) occur in developing countries, where access to healthcare workers can be limited.[13] Women die as a result of complications during and following pregnancy and childbirth; however most of these complications are preventable or treatable.[14] One of the leading causes of maternal death, post-partum hemorrhage, can kill a healthy woman within hours if she is unattended. But injecting Oxytocin immediately after childbirth reduces the risk of bleeding and saves lives.[15]



Patient Adherence Opportunities

For drugs requiring self-injection, a low-cost single-dose format* that requires very little training could potentially make adherence more likely. Crucial for regimens such as TB and potentially other diseases in countries or populations where cost is a critical factor.

For many patients, adhering to a medical protocol can be challenging due to many factors, such as cost, but self-injection (when approved at the option of regulatory authorities) can address some of those issues.

For example, the ability to self-inject contraceptives can encourage continuation of contraceptive coverage as it addresses some of the reasons why women discontinue use, such as travel expenses, long distances to the clinic, and long waits at the clinic.[16]

For young women and adolescents, who often have higher rates of contraceptive discontinuation, and also highly value their privacy, self-injection can offer independent and discreet contraception use over a longer period of time.[17]

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Wider Coverage of Injectable HIV PrEP Treatments

New injectable HIV therapeutics are in development that will require injections every month or two. The option for self-injection (where permitted at the option of regulatory authorities) or injection by community health workers dramatically expands access.

New antiretroviral (ARV) treatments in injectable format are in development for treatment of HIV and have been well received by patients in a trial. Patients preferred receiving treatment every four or eight weeks with the injectable format rather than taking daily pills, which also helped them avoid what they felt was a daily reminder of their HIV status.[18]

Trial participants found the new dosing protocol more convenient and more private.[19] The participants also said that the injections were more convenient and made for easier adherence to their HIV treatment regimen.[20]

WHO Seeks Improved Coverage, Based on Wider Access to Injectable Polio Vaccines

WHO has called for a global changeover from oral to injectable polio vaccines. As that transition occurs, ApiJect Prefilled Injectors* could potentially support it.

In May 2012, the World Health Assembly of WHO declared poliovirus eradication to be a programmatic emergency for global public health.

Under this plan to achieve and sustain a polio-free world, it recommends that the use of Oral Polio Vaccine (OPV) must eventually be stopped worldwide, and that at least one dose of Inactivated Polio Vaccine (IPV), an injection, must be given in addition to OPV, to protect against type 2 poliovirus and to boost population immunity.[21]

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Surge Production in Medical Crises

When epidemics break out, cities or countries need to ramp up in a hurry to get vaccines or medicines to a broad population. Making glass vials requires a lead time of up to 6 months or more. Instead, a single BFS manufacturing line can start producing up to 25,000 finished units* an hour within days of regulatory clearance of the vaccine or medicine on the line.

The traditional aseptic filling process can require up to 12 steps, involves numerous people, and can take months to complete, even when the bulk vaccine is available.[22] These requirements are less than ideal when addressing epidemics. ApiJect's manufacturing process has the potential to reduce risk of human contamination, and could potentially result in fewer raw materials needed, smaller facilities required, less use of utilities such as water, and fewer steps in the production process because separate stations for cleaning, sterilizing, and filling aren't necessary.[23]

This simplified process is potentially valuable when rapidly producing and shipping medicines and vaccines to save lives.

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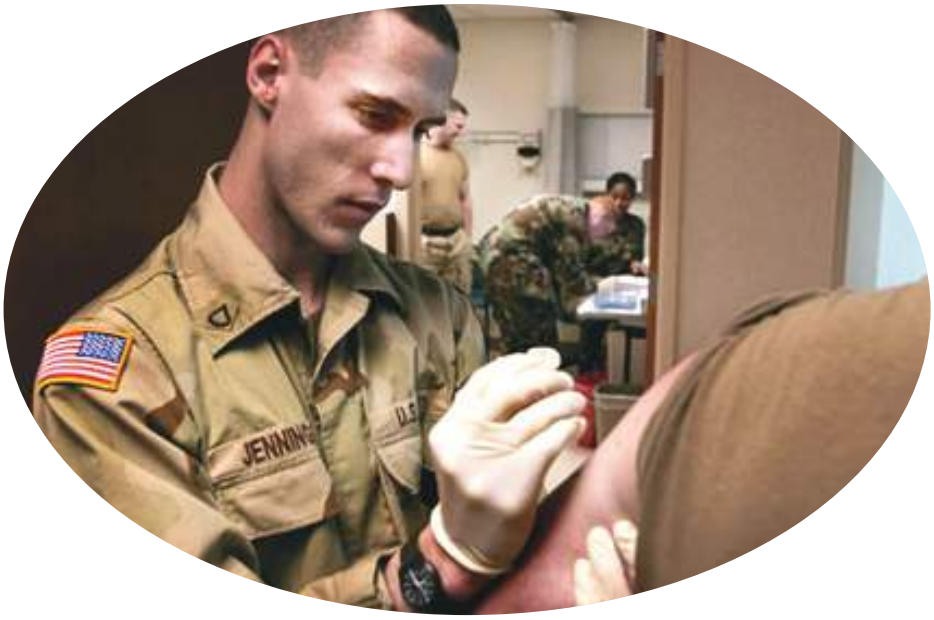

First Responders Need Fast Help

Soldiers, police and firefighters don't always have a medic, doctor or clinic nearby when injury occurs. An easy-to-use, prefilled single-dose injector* could potentially support first responders' needs to carry medicine for immediate injection, and patients' needs for immediate treatment.

On-call emergency workers operate in the field without all of the resources and equipment that a hospital or clinic provides. Having to measure and withdraw the precise amount of medicine from a glass vial and then change needles to inject patients in need while in a high-pressure situation adds complexity to an already stressful circumstance.

The convenience of a planned prefilled, single-dose injection device* that could be quickly scaled when speed is critical, coupled with the high quality and durability of the BFS format, could potentially offer benefits for emergency personnel and their patients.

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Allergies and Anti-Opioid Applications

Epinephrine and Narcan are very expensive in today's formats. With additional R&D, and subject to the need for approval from regulators, injections using ApiJect Prefilled Injectors* could become available, requiring smaller doses and resulting an economic alternative format.

Costs of medicines such as Epinephrine and Narcan have steadily risen, resulting in them being less available, just as the need for them increases.[28] Using single-dose, prefilled BFS injectors, such as ApiJect's,* could potentially provide more coverage due to their more affordable manufacturing costs.[29]

The potential for dose sparing, along with the convenience of a prefilled single-dose could potentially benefit patients and health workers delivering medicines in emergency situations, such as when administering Epinephrine and Narcan.

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Veterinarians and Pet Owners

Veterinarians spend much time dosing injections for the world's 500+ million pets. ApiJect Prefilled Injectors* could potentially eliminate that step, saving time. And, if the law permits and regulators approve, vets could have the option to prescribe injections for pets, given by owners at home, so more pets could potentially get treated.

Injecting pets with needed medicine and vaccines can be a difficult task. This especially true for aggressive pets or pets with a history of abuse that don't trust humans. Reducing the steps required for a vial and syringe injection, could potentially make it easier for the vet administering the injection and less stressful or traumatizing for the animal.

Additionally, permitting pet owners to care for their pet in their home environment by injecting their pets themselves – at the option of regulatory authorities – would not only be more convenient, but also a better experience for the pet. These interventions could potentially support coverage of more pets, help reduce the number of pets that otherwise would go unvaccinated or untreated.

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Animal Health on Small Farms

Worldwide an estimated 70 billion farm animals are raised for food. In low-and middle-income countries, far fewer farm animals receive medicinal injections than in the West. A prefilled single-dose device* could potentially help small subsistence farmers and disadvantaged families treat animals showing signs of illness.

Farmers in low- and middle-income countries are often on their own when it comes to guaranteeing their farm animals' health and productivity. When treating a sick animal, it is imperative that the proper dose of medicine is used, as too much of the medicine can kill an animal, while too little won't cure the disease ailing the animal.[30]

If a prefilled single-dose device such as an ApiJect Prefilled Injector* were available to farmers and approved at the option of regulatory authorities, could potentially assist farmers to support the health of their animals, on which they depend for sustenance and livelihood.

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ApiLabs

How We'll Manufacture a More Economically Efficient Injection Delivery System, Without Compromising Safety

ApiJect is reimagining how well-established technology can be combined in the ApiJect Prefilled Injector* to deliver reliable aseptic quality, maximum safety and maximum population coverage for injectable drugs.

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Low- and middle-income countries typically have been forced to choose between maximum coverage and maximum safety for their injectable vaccines and medicines.
An innovative new injection system* is planned to provide both.

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The medical device industry said it couldn't be done.

For decades, the world's healthcare organizations have faced a difficult choice, especially in low- and middle-income countries.

- If safety was their priority, they chose prefilled syringes that deliver precisely the right dosage and cannot be reused or contaminated. However, prefilled syringes cost more, which means covering fewer patients.
- If they wanted to use their limited budgets to cover the largest possible number of patients, they needed the injection format with the lowest cost per dose delivered. That meant reusable syringes and multi-dose glass vials.

Health experts believed it would be impossible to achieve the safety of prefilled syringes, at a total delivery cost lower than that of multi-dose glass vials.

The ApiJect Prefilled Injector* is planned for efficiency and safety.

ApiJect's new injection platform is planned to provide the safety of a prefilled syringe at a cost per dose delivered comparable to that of injections from multi-dose vials.

What's more, each ApiJect production line is planned to run BFS machines that fill and finish 25,000 BFS Containers per hour with lead times of only 1-3 days, to support potential rapid scaling and supply of Prefilled Injectors.

How is this possible?

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Introducing Blow-Fill-Seal manufacturing.

Blow-Fill-Seal (BFS) manufacturing is a well-established technology for packaging pharmaceuticals and other sterile products.

Every year, the BFS industry produces 50 billion filled and finished units of sterile biological agents such as eyedrops, nasal sprays and the like, packaged in a wide variety of bottles and containers.

BFS can be used to make Prefilled Injectors* by attaching a Needle Hub to the top of the BFS Container.

ApiJect's partner, the German company Rommelag®, invented BFS technology and remains the world's leader in the field.

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This one small BFS line can produce, fill and finish 25,000 containers per hour for prefilled injectors.

This is a BFS manufacturing machine. The larger unit at left heats the raw plastic, forms it into multiple containers simultaneously, fills each container with vaccine, cools it, seals it, trims it and sterilizes it.

The resulting belt of containers is then fed into the smaller machine at right, which trims off any excess plastic.

The entire process takes 3-7 seconds, start to finish. (Needle Hubs are prefabricated elsewhere and shipped to the point of care.)

Compared with the factory-sized space requirements for manufacturing glass vials and syringes in high numbers, both units of the BFS machine require a very small footprint.

STEP 1

Acquire the needed raw materials.

The first step in BFS manufacturing of ApiJect Prefilled Injectors* is to acquire bulk supplies of the needed components:

1. Raw plastic resins to be formed into injectors.
2. API's (Active Pharmaceutical Ingredients: the medicines or vaccines that will be packaged in the prefilled injector, subject to regulatory approval in each case).
3. Needles (each needle is planned to be contained in ApiJect's proprietary Needle Hub,* which will be manually attached to the prefilled Container by the caregiver at the point of care).

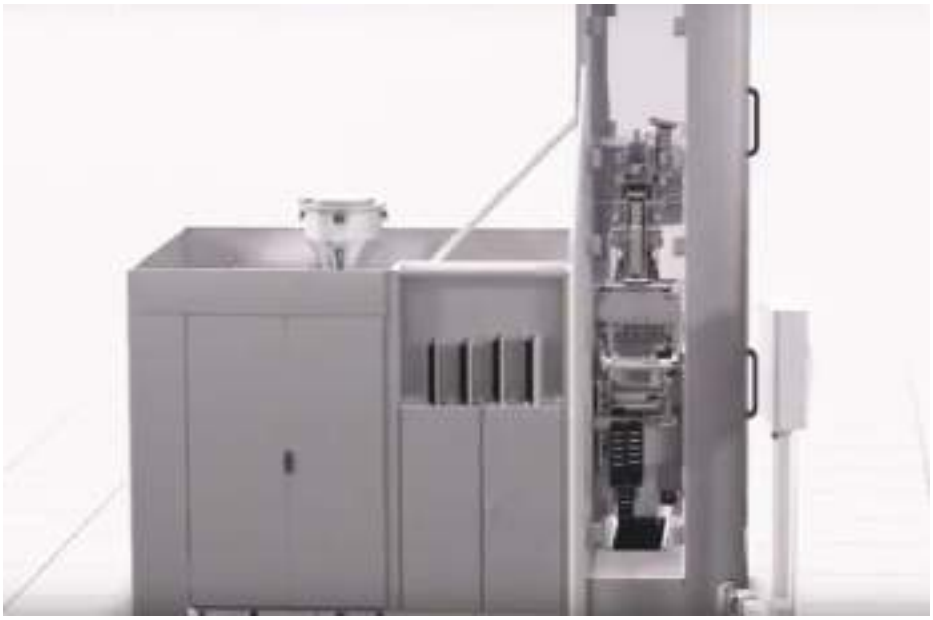
STEP 2

Stock the overhead storage silo with liquid vaccine.

Liquid vaccines are stored in silos above the BFS machine.

At the proper time during the manufacturing process, the vaccines will pour down from the silos, through a manifold, and will be fed directly into the newly formed injectors, inside the BFS machine.

STEP 3



Load the pharmaceutical-grade plastic resin and heat it.

Raw resin for BFS Container production is also fed into the BFS machine. To aseptically package 25,000 doses an hour, a total of 25 kilos of resin must be on hand.

In this side view of the BFS machine, the square unit on the left half of the image is where resin is heated to prepare for the extrusion of the parison. (A parison is a molten plastic tube that will become a container or injector.)

The square unit at right also contains cooling and heating equipment for parisons and molds.

STEP 4

IMAGE COURTESY OF ROMMELAG®

Form the parisons (molten tube shapes).

Heated plastic is extruded from the top of the machine. The molten plastic slowly falls downward, pulled by gravity, into the "Class A" clean space (the zone around the gold colored section).

Using positive air pressure and vacuum, the falling molten plastic is formed into a series of open tubes, called a parison.

(The parison is shown at top center of image, appearing as white funnel shapes: wide at the top, narrow at the bottom.) A single parison contains multiple funnels that are formed into multiple containers or injectors.

STEP 5

IMAGE COURTESY OF ROMMELAG®

Close the head (upper) mold to form the injector shape.

To close the open container shapes, two mobile, parallel bars in the horizontal table converge at one end of the molten plastic parisons.

The inner faces of these parallel bars contain the molds that will shape the molten plastic into the desired container, such as a bottle or an ApiJect "two-chamber" injector.*

STEP 6

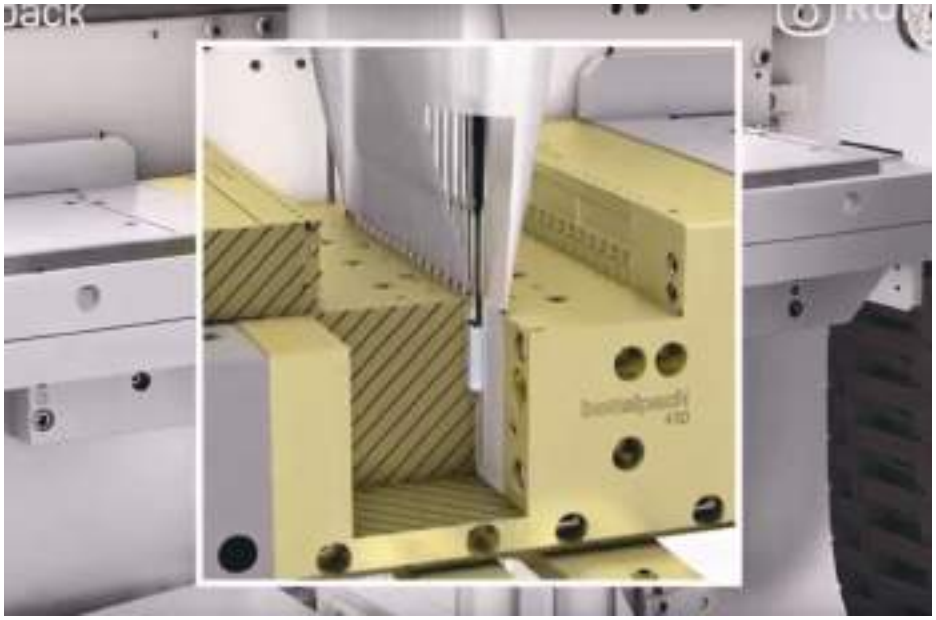


IMAGE COURTESY OF ROMMELAG®

Cool the molten plastic.

At virtually the same moment that the mold creates the injector shape, the mold's inner face plates are instantly chilled from 75° C to 20° C.

This instantly molds the parison into its permanent shape as a series of ApiJect "two-chamber" BFS Containers.*

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STEP 7

IMAGE COURTESY OF ROMMELAG®

Fill the BFS Container with vaccine or medicine.

Once the planned future injector* has been given its shape and has been properly cooled, the time has come to fill it.

The next step in the BFS process is filling the Container with the drug. But by quickly cooling the shaped resin and pre-cooling the drug product, the short burst of heat upon initial filling should not harm the vaccine or medicine.

The vertical black "screwdriver" shape in the center of image is a "filling needle." It extends downward from the top of the machine, into each BFS Container.

As always, subject to regulatory approval, liquid vaccine flows down through this needle to fill the injector with the precise dosage that is required for that particular pharmaceutical agent.

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STEP 8

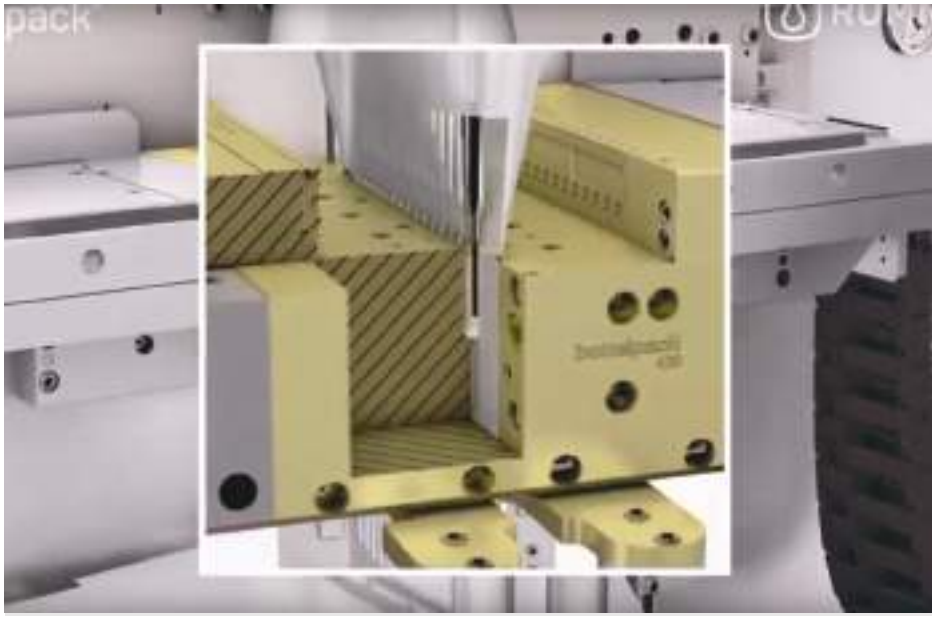
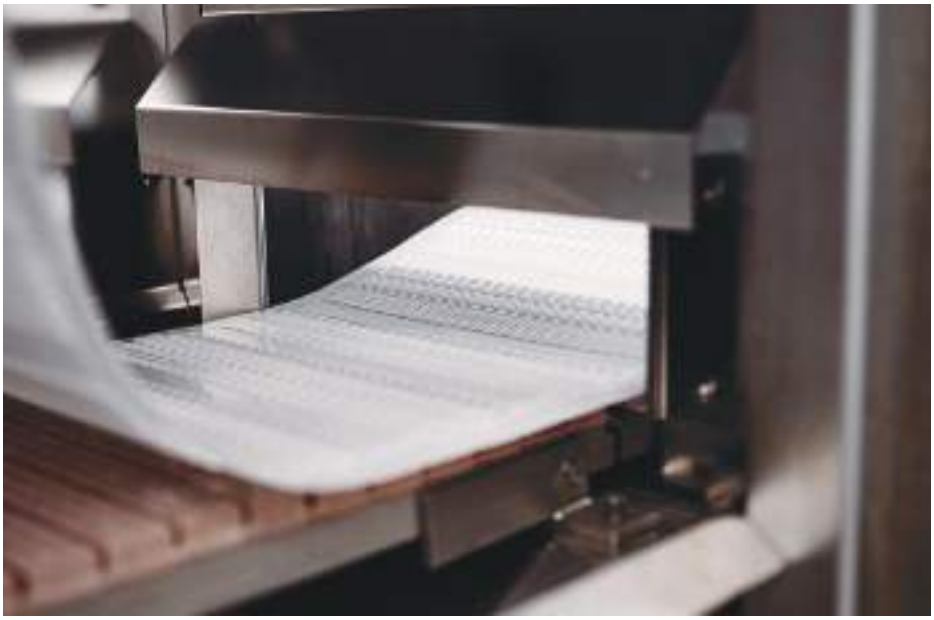


IMAGE COURTESY OF ROMMELAG®

Withdraw the filling needle and seal the Container's other end.

After the Container is filled with vaccine, the needle is withdrawn and the head mold seals the open end of the Container.

STEP 9



Feed the resulting belt of BFS Containers into the adjacent die-cutting machine.

A continuous belt of prefilled containers, in strips of multiple containers in a row, scrolls out of the bottom of the main BFS manufacturing machine.

This belt moves upward in a continuous loop from the main machine to feed the injectors into the smaller die-cutting machine, located immediately adjacent.

STEP 10

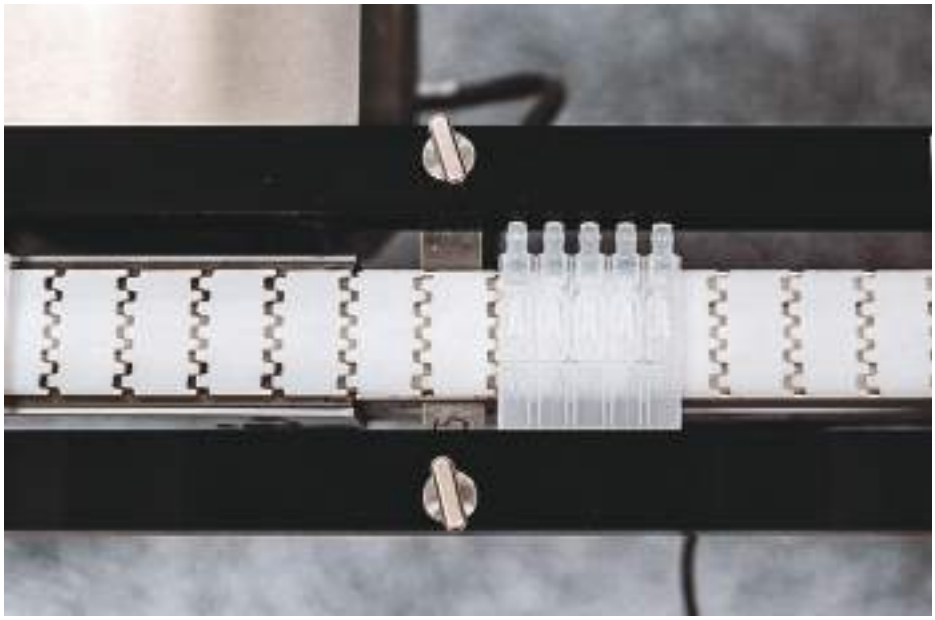
IMAGE COURTESY OF ROMMELAG®

De-flashing (removing excess plastic) is performed by a Separator machine.

The de-flashing machine cuts the continuous belt of thousands of prefilled containers into individual units or strips of the desired number.

For example, the Separator could produce a series of single containers, or a strip of 5, or 6, or 10 containers that are presented in a single small sheet of plastic.

STEP 11



Vending of final product.

After de-flashing, the trimmed finished products exit the machine. In this case in a series of 5-container “cards” were produced.

STEP 12

Affix the connector mount and Needle Hub.

Needle Hubs* and connector mounts are prefabricated in a separate location.

Hubs, mounts, and Connectors are shipped to the same destination, where they are assembled manually in seconds by the caregiver at the point of care, just prior to injection.

Assembly is accomplished with a simple "push-to-activate" step.

*Products shown for informational purposes only, not for use in product promotion.
ApiJect's Prefilled Injector and other products have not been reviewed or cleared by FDA or other regulatory authorities for distribution.

STEP 13

Sterilize the finished product.

Sterilization does not require a separate step. The BFS Container* is already aseptic because it is manufactured in a "ISO Class 5" clean space inside the BFS machine.

Needle Hubs* are pre-sterilized using Ethylene Oxide Processing (EtO). This procedure is widely used for healthcare devices and instruments.

EtO exposes products to a sterilizing gas under vacuum in a sealed chamber.

STEP 14

Inspect for quality.

Quality Assurance is not a separate process, either. Much like sterilization, it is integrated directly into production.

QA checks occur at 10 to 15 separate points throughout the BFS manufacturing process.

High-speed cameras inside a Cosmetic Inspection Machine* capture critical images that are instantly computer-scanned and analyzed. The entire process takes just milliseconds.

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STEP 15

Package for shipment.

The finished components for prefilled injectors* are labeled, wrapped, cartoned, and boxed for shipment, using standard automated systems.

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ApiJect's Prefilled Injector and other products have not been reviewed or cleared by FDA or other regulatory authorities for distribution.

ApiLabs

BLOW-FILL-SEAL: Manufacturing at a glance

1. EXTRUDING

The polymer parison is extruded from granulate and positioned inside the open mold.

2. BLOWING

The mold closes and, in doing so, welds the base. The mandrel is positioned on the neck of the container and blows sterile air into the parison to create the desired shape. Small containers are created using a vacuum.

3. FILLING

The exact amount of filling as measured by the dosing system is fed into the container via the mandrel.

4. SEALING

Once the mandrel is removed, the head mold comes together to form the desired closure type.

5. DEMOLDING

Opening the mold releases the container from the system and the next cycle begins.

The ApiJect Prefilled Injector* is designed to be potentially the first-ever injection format combining all the advantages of prefilled syringes with the economic efficiency and rapid production of aseptic Blow-Fill-Seal manufacturing.

ApiJect believes that every healthcare system can deliver full equity without compromising patient safety.

*Products shown for informational purposes only, not for use in product promotion.
ApiJect's Prefilled Injector and other products have not been reviewed or cleared by FDA or other regulatory authorities for distribution.

Injection Technology for Vaccines and Medicines: Past Evolution, Future Landscape

With innovations such as Micro-Array Patches (MAPs), multi-nozzle jet injectors, BFS cPADs and others, injection technologies are moving toward a historic shift.

Injections of vaccines and medicines have taken two different paths. Vaccine delivery has largely shifted to Auto-Disable syringes and Vaccine Vial Monitors. Buyers sometimes pay slight premiums for greater total effectiveness.

Yet for (non-vaccine) medicines, many countries still buy the lowest-cost option: traditional syringes and multi-dose vials.

These disposable syringes should be discarded after one use. Tragically, many get reused repeatedly. This saves money, but it also creates cross-contamination, spreads infections and – according to WHO – kills up to 1.3 million people a year. [1]

Injection is one of the most effective ways to administer licensed vaccines and countless medicines.

Most vaccines, along with many medicines, are administered by syringe, but there are other methods.

According to *Plotkin's Vaccines,* the field's standard reference work, all liquid vaccines and many medicines are typically given to patients:

1. by needle and syringe; or
2. through oral delivery; or
3. via nasal spray.[2]

As for shipping, nearly all vaccines ship as liquids in single- or multi-dose vials (along with empty syringes), or as liquids in prefilled syringes. A few vaccines and medicines are shipped in ampoules. Also, some vaccines – referred to as "lyophilized" vaccines – are freeze-dried before shipment for greater stability. They must be reconstituted into liquid at the point where they are administered to a patient. This is accomplished by mixing the dry (lyophilized) vaccine with a liquid diluent.[3]

To administer vaccine or medicine using traditional syringes and vials, the administrator first uses the syringe's needle to suction liquid from the vial into the syringe barrel, withdraws the needle from the vial, and then uses the same needle to inject the liquid into the patient.

A different technology is the prefilled syringe, supplied to the point of care already loaded with a single, correctly-sized dose of the liquid to be injected. No onsite filling is required; no glass vials are needed.

An ampoule is a sealed, prefilled capsule containing a fixed dose or doses of liquid vaccine or medicine. They're opened by breaking off the neck of the device.

New injection technology is needed because reused syringes and contaminated multi-dose vials lead to 1+ million deaths a year.[4]

Traditional vials and syringes save countless lives, but also put lives at risk.

Over the decades, traditional syringes, filled with medicines and vaccines from glass vials, have saved countless lives. But they also cost many lives through cross-contamination and infection in clinical settings.[4]

In some low-resource settings, syringes are "cleaned" and reused over and over. When a contaminated syringe is filled from a vial, it contaminates the vial's contents and invisibly spreads diseases such as HIV and hepatitis.[5] According to the World Health Organization: "A 2014 study sponsored by WHO, which focused on the most recent available data, estimated that in 2010, up to 1.7 million people were infected with hepatitis B virus, up to 315,000 with hepatitis C virus and as many as 33,800 with HIV through an unsafe injection."[6]

Syringes are easily contaminated. When an administrator withdraws the needle from a patient, microscopic blood droplets are pulled from the patient into the syringe barrel. Boiling the syringe in water or washing it in alcohol cannot decontaminate it.

If the first patient had a blood-borne disease, the next patient injected by that syringe risks getting the disease pathogen with the injected medicine or vaccine. Filling the contaminated syringe from a vial also contaminates the remaining vial contents.

But the basic technology for injecting vaccines and meds has changed very little in 165 years. It's still about a syringe and a glass vial.

Syringe design has evolved relatively little since its invention.

For 165 years the global medical establishment has relied upon the same basic technology for injections. Small glass vials of medicines or vaccines are distributed to points of care around the world. From these vials, syringes are carefully filled.

Basic syringe design and functionality have remained largely the same since the device was invented. A hypodermic needle withdraws the liquid from the vial into the syringe barrel. The same needle then punctures the patient's skin; a plunger pushes the vaccine or medicine out of the barrel, through the needle, into the patient. The plunger is pulled back, withdrawing the needle from the patient.

Three lengths of needle are commonly used to inject vaccines and medicines: intradermal, subcutaneous, and intramuscular. Each length penetrates to a different skin layer.

Intradermal injections are delivered into the dermis, or the skin layer underneath the epidermis (which is the upper skin layer). Subcutaneous injections are administered in the fat layer, underneath the skin. Intramuscular injections are delivered into the muscle.

Syringe materials have evolved, but the vials containing vaccines and medicines are still made of glass.

1850 Metal

1930 Glass

1980 Plastic

There are many challenges associated with using glass vials for vaccines and medicines.

While syringe design has not evolved greatly, there has been marked evolution in materials. Early syringes were made of metal. By the 1930s, glass barrels were the norm. Plastic syringes became widespread starting in the 1990s.

However, well into the 21st century, the vials are still made of glass. Plastic vials were tried, but they were too easy to accidentally puncture with the needle when filling a syringe. Such punctures can worsen existing problems of waste and contamination that are inherent risks with multi-dose vials. Glass has many drawbacks that add to its cost and reduce its ability to be support rapid, population-level immunizations.

Vials for vaccines and medicines are produced through an automated, factory-scale glass blowing manufacturing process that is slow and costly when compared with advanced plastics manufacturing.

Glass manufacturing is one of the most energy-intensive industrial processes; it also produces high levels of industrial waste. Vials and syringes frequently get broken in the factory and during transport, costing companies millions of dollars. In a recent 5-year period, glass breaking and flaking led to 100+ million vials or syringes being pulled from the market.

High-income countries use single-dose vials because they're safest. But other countries buy the lowest-cost format: multi-dose vials.

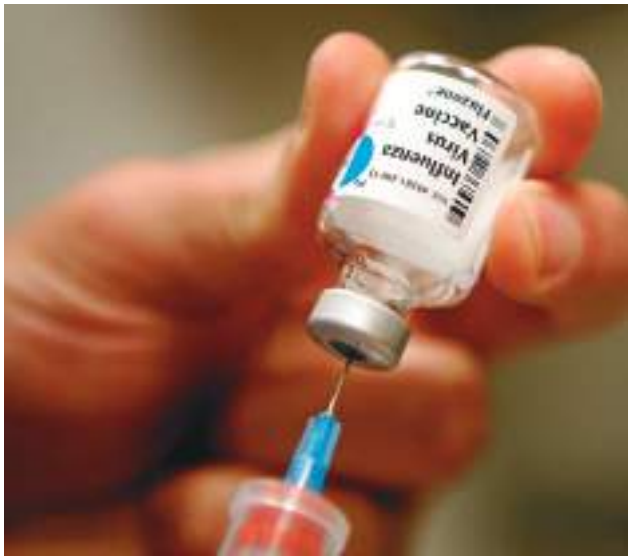
Understandably, health ministries seek the maximum coverage possible within the scope of their limited budgets.

For vaccines, reusable syringes in low- and middle-income countries have largely been supplanted by single-use, Auto-Disable syringes. This format is the only type purchased by UNICEF and Gavi, which support vaccine administration in many nations. But regardless of syringe type, most Low- and Middle-Income Countries (LMICs) purchase vaccines and medicines in multi-dose vials because it's more economical to buy them like everything else – in larger containers.[43]

Lower cost is why the 10-dose glass vial still accounts for between 75% to 80% of global volume of injectable vaccines. In some areas, the rate is 90%.[7]

Arguably, the official cost difference between a single-dose vial and a 10-dose vial is just the tip of the iceberg. The practical truth is that it's far cheaper to buy one 10-dose vial and one traditional syringe, then refill and reuse that syringe 10 times despite the safety risks entailed, than to buy 10 syringes and 10 single-dose vials. Unfortunately, experience shows that in many LMICs, reuse of syringes for injectable medicines remains a common practice – and too often, for vaccines as well.

According to the WHO's Dr. Benedetta Allegranzi, Lead for the WHO "Clean Care is Safer Care" program, "Over 70% of injections are given with reused syringes and needles in the developing world."[8]



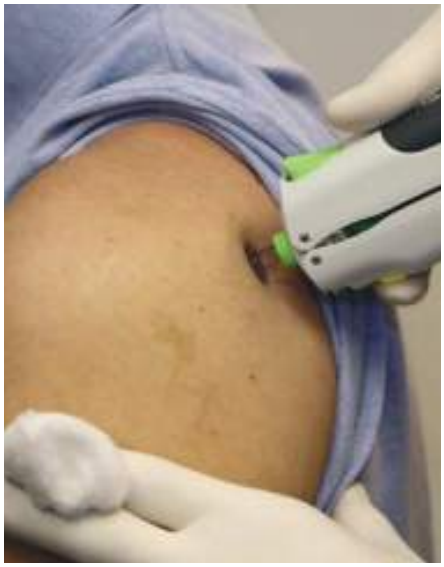
Today many new technologies are being
New technologies include advanced jet

Broad-based innovation comes to vaccine and medicine administration.

A broad spectrum of new technologies for administering vaccines and medicines is now emerging into the healthcare field.

These technologies "represent paradigm shifts in manufacturing and healthcare worker use," say experts. New technologies for vaccine and medicine administration fall into 5 major categories: Modern Jet Injectors; Micro-Array Patches; Other Trans-Cutaneous delivery; Mucosal Vaccination; and cPADs.

> "New technologies have the potential to eliminate or reduce restrictions to vaccine flow, increasing the capacity and efficiency of immunization programs."
>
> *– Plotkin's Vaccines*

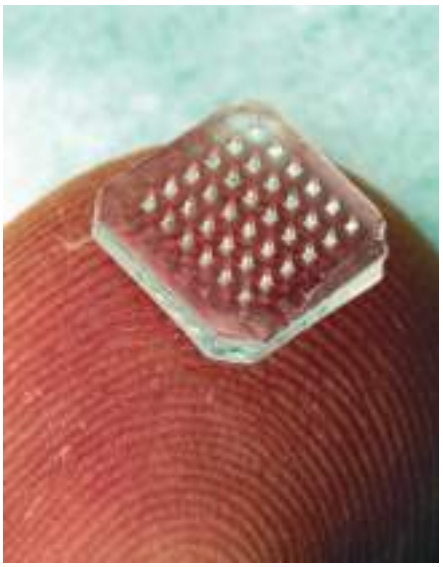


1. Modern Jet Injectors

A handheld format that forces liquid through a tiny nozzle under high pressure, producing a concentrated stream of vaccine that penetrates the patient's skin without needles.[10]

Traditional (multi-use nozzle) jet injectors have been deployed to administer hundreds of millions, possibly billions, of vaccine doses for mass campaigns in humans.

Modern jet injectors with single-use nozzles are used in delivery of flu vaccine and inactivated polio vaccine.



2. Micro-Array Patches

Vaccines may be coated onto arrays (rows) of solid, pointed projections that are so short, they are not classified as needles.

The tiny arrays go on stamp-like Micro Array Patches (MAPs). Applied to the patient's skin by hand or by using an applicator, they release vaccine and medicine.

Still in an early stage of development, this technology has been tested in two European nations.

developed to replace traditional syringes. injectors, Micro-Array Patches and cPADs.

3. Other Trans-Cutaneous

This category is subdivided into a dozen different types including electroporation; powder injection; and more.[14]

The purpose of these technologies is shallow delivery of vaccine into the dermis or epidermal layers of the patient's skin, a goal that requires use of the Mantoux method when traditional syringes are used.

4. Mucosal Vaccination

Technologies for introducing vaccines directly into respiratory, gastrointestinal and genito-urinary tracts.[15]

This enables precise targeting against infections of those areas.

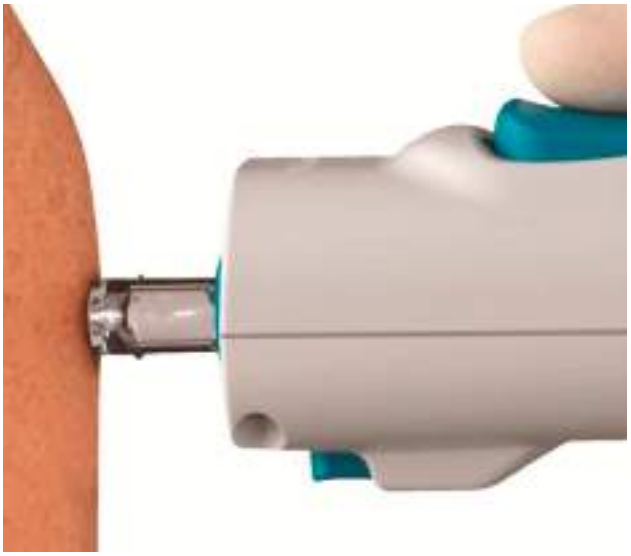
Delivery formats in this category include a range of devices and methods, such as oral administration of liquid drops, sublingual spray or gel delivery, nose sprays, nasal drops, nasal nebulizers and intranasal dry powders.

5. cPADs

"cPAD" indicates a "compact, Prefilled, Auto-Disabling" syringe for single-dose injection. Liquid vaccine or medicine is contained in a soft plastic "squeeze-bottle" container with attached needle.

Rather than the traditional syringe's Auto-Disable plunger, a cPAD's disable feature could be a locking valve or a collapsible container that, once emptied, is virtually impossible to refill.

Jet injectors have been deployed since the 1950s, originally with reuseable (multi-use) nozzles, in large-scale vaccination campaigns.



They are also known as jet gun injectors, air guns and pneumatic injectors.

Over the past 50 years jet injectors have been used in mass campaigns against smallpox, swine flu and other diseases. Total injections in these campaigns have numbered in the hundreds of millions or in the billions.[16]

Jet injectors for intradermal delivery have several benefits. They enable health workers to deliver doses quickly to a high number of patients.

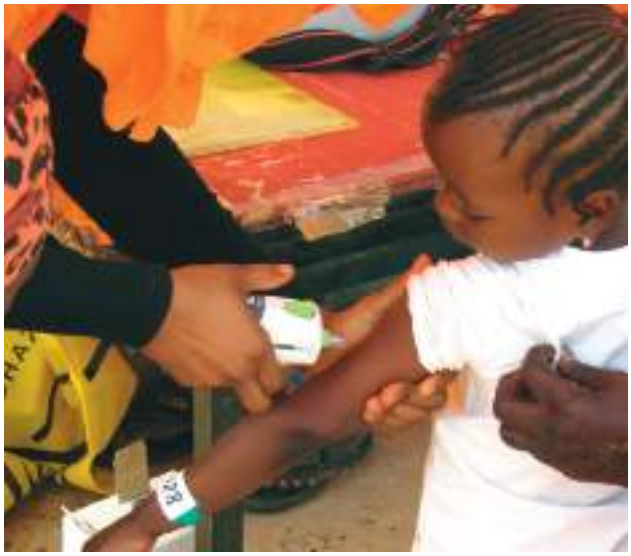
They are simple to use, eliminate needlestick injuries and make it possible to deliver off-the-shelf vaccines without reformulation.

Patients like jet injectors because of the lack of a needle, which is psychologically appealing.[17] And, according to some reports, needle-free injections inflict less actual pain than needle-based devices, also a popular feature with patients.[18]

But the original technology was not without drawbacks. "Multi-use Nozzle Jet Injectors…have been linked to iatrogenic (clinical-caused) transmission of blood-borne pathogens," according to *Plotkin's Vaccines*.

Starting in the 1990s this problem was addressed with the development of Disposable-Syringe Jet Injectors (DSJIs).[20] Manufacturing a DSJI syringe and durable injector delivers a higher margin of safety, although it also imposes higher costs than traditional vial and syringe platforms.

Modern jet injectors use disposable (single-use) nozzles to overcome the safety challenges of previous technology versions.



Decades of continuing R&D have addressed safety challenges with jet injectors.

Modern jet injectors have been used widely in the U.S. for influenza vaccinations in mass market retail venues such as Walmart.

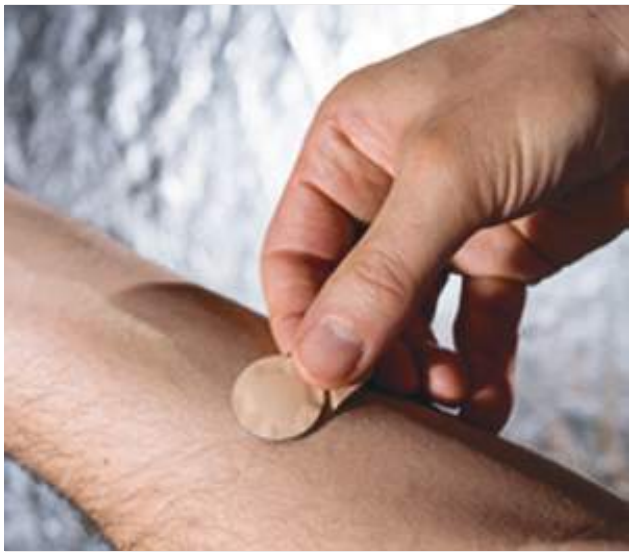
They have recently been purchased in a multi-year quantities (along with along with millions of refill cartridges) by WHO for its Global Polio Eradication Initiative in Bangladesh, Cuba, Gambia and Pakistan.[19]

Despite their higher expense compared to the purchase price of traditional vial and syringe platforms, Disposable-Syringe Jet Injectors compare favorably in terms of final delivery cost per dose, when the cost model assigns the cost of spreading disease through unsafe injections to the vial and syringe method, and only if the accounting method is careful to give DSJI's credit for avoiding these costs.[21]

And, although the high cost of DSJI manufacturing may be amortized when it's spread over populations where high levels of vaccination occur, cost may be "prohibitive" in areas where volumes of vaccinations are low, states *Plotkin's*.[22]

Newer models have reportedly overcome the health problems associated with earlier generations of jet injectors.[23] However, the current technology comes with greater complexity and imposes costs for capital equipment, maintenance and disposable components that may be challenging in some markets.

Micro-Array Patches (MAPs) offer an innovative alternative to traditional vial & syringe injection technology.



This technology is also known as a microneedle patch.

Micro-Array technology features a patch that is placed on the patient's skin to deliver vaccine through rows of sharps, sometimes called microneedles. Hand pressure or an applicator presses the sharps into the skin, where the vaccine coating rapidly dissolves. In some formats, the rows of sharps themselves also dissolve.[24]

MAPs are sometimes described as having "micro-needles." But MAPs are also described more accurately as "needle-free," because the sharps that they deploy are so small that, technically, they do not qualify as needles. Definite benefits accrue with MAPs. To many patients, a patch seems less scary than more obviously needle-based technologies. MAPs can be shipped by mail in dry format and self-administered by patients or administered by healthcare workers with very little training.[25]

PATH has noted that Micro-Array Patches can be considered "an easy-to-use and discreet delivery method." For this reason, said PATH, Micro-Array Patches could enable wider self-administration of vaccines and medicines in a broad range of outpatient settings.

"Moreover, some patches could be formulated for long-acting, sustained delivery to help reduce the frequency with which they need to be re-administered," noted the organization.[26]

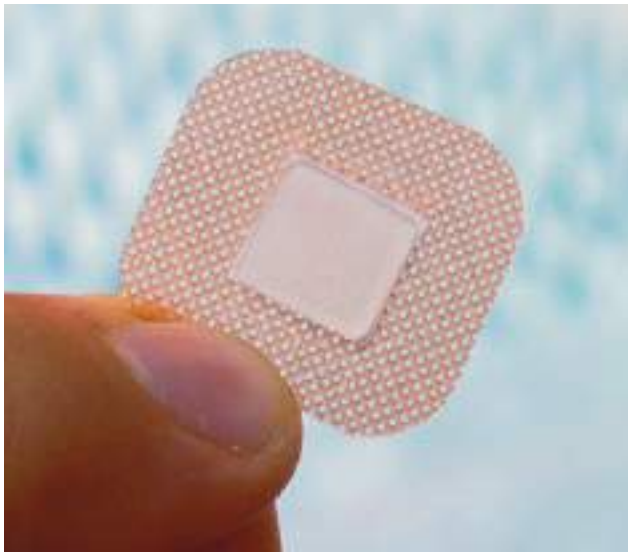
Micro-Array Patches have generated great excitement. Major R&D funding is being deployed from numerous sources.

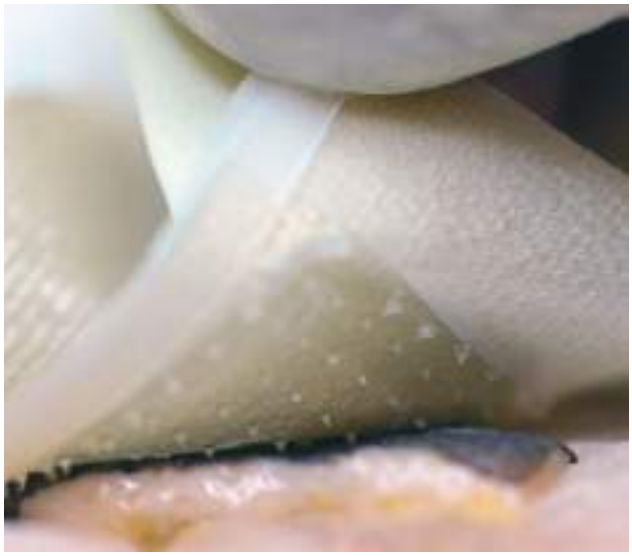
MAPs have been touted by some as a major part of the future of vaccine delivery.

Micro-Array Patches are widely believed to be a "potential[ly]…transformative technology for vaccine delivery."[27] The level of interest and excitement generated by MAPs may be gauged in part by a steady stream of R&D funding events.

These include a $10 million grant from the NIH for a Microneedle Vaccine Patch in 2010;[28] a $9.4 million grant from USAID in 2017;[29] and others including support from the Gates Foundation for HIV prevention using MAPs by a subsidiary of GSK (Glaxo-Smith-Kline). A significant body of preclinical research has been done on the use of Micro-Array Patches for vaccines. Some flu vaccines have undergone phase 2 clinical trials with MAPs or early-stage clinical trials are in progress for other vaccine applications.[30]

Public and media attention have also been highly enthusiastic. Headlines such as, "Novel drug delivery system has game-changing potential to reduce rates of HIV infection," accompanied the 2017 PATH funding announcement.[31] Microarray patches are a dry presentation format that enables some vaccines to remain potent for up to a year without refrigeration, say advocates. Supporters also point to less need for storage space, transport space and user training.[32] Finally, for some vaccines, MAPs allows less antigen to generate effective results so a specific amount of vaccine translates into more doses with MAPs than with other formats.[33]





According to WHO in 2018, MAPs are 8-10 years away. Much testing remains to be done; and, many questions remain unanswered.

From cost and efficacy to regulatory issues, there is much to learn.

Although Micro-Array Patches have been talked about (and funded) for more than a decade, as of 2018 they remained "in an early stage of development for use with vaccines," according to *Plotkin's Vaccines*. "Challenges include generating clinical evidence and scaling up manufacturing processes."[34]

In practical terms, this means among other things that healthcare professionals and device developers simply don't know what kind of real-world reception and results MAPs might generate. There are unanswered questions about many issues. Such as…

Will MAPs demonstrate efficacy with each candidate vaccine?

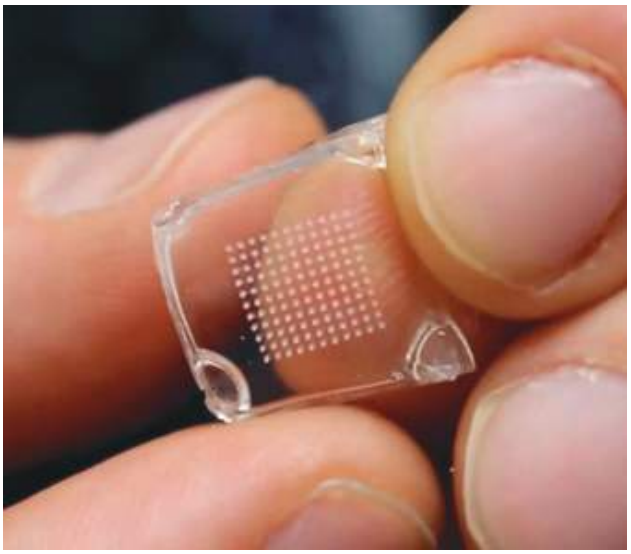
Will syringe manufacturers be willing to change from the 165-year-old needle and syringe format to something so radically different?

What will be the final costs of manufacturing and per-dose delivery? Will regulators approve?

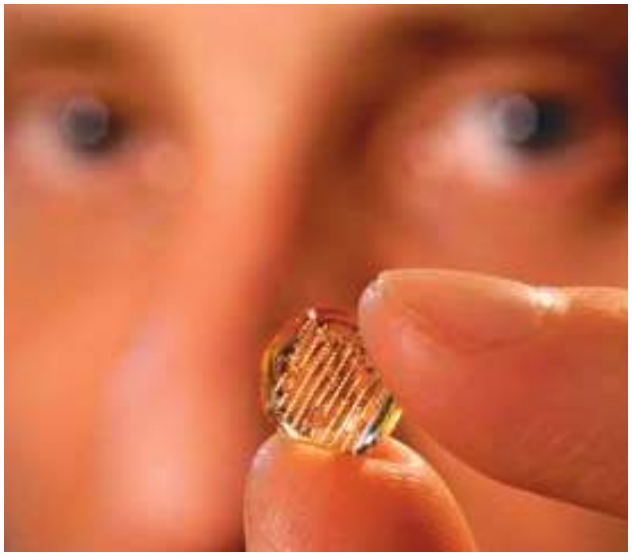
How long does a patch need to stay on the patient?

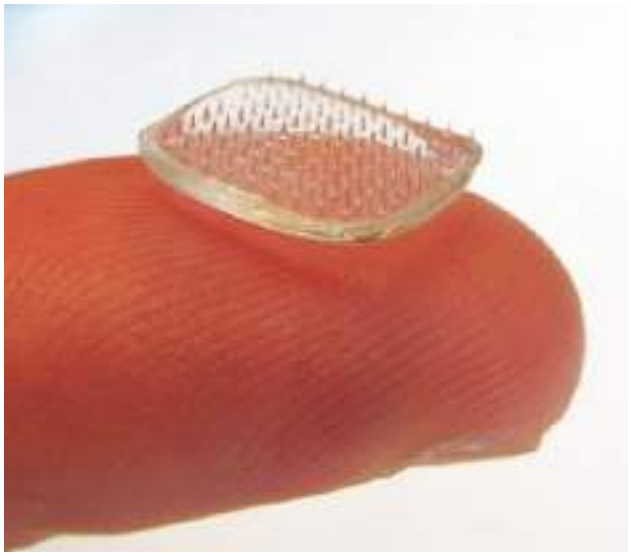
Does it need more time than injections given by a traditional syringe (30 seconds)? Will children, or their mothers, take it off too soon?

Today no one can answer these questions with certainty.



Cost will be a major factor in the market acceptance of Micro-Array Patches. Estimates of future prices vary widely.





A number of issues will impact MAPs cost.

"Preliminary cost modeling by PATH has found that the costs per dose for an IPV (inactivated poliovirus vaccine) patch are likely to be higher than conventional IM or ID injection, but this may be offset by lower delivery costs if the technology enables dose-sparing or storage at ambient temperatures," reported one study in *Vaccines*.[35]

According to WHO, factors that could help "reduce the cost of vaccine delivery" with MAPs include "increased vaccine thermo-stability, reduced packaging volume, ease of delivery, safer administration and disposal–possibly enabling delivery…by minimally trained health workers and volunteers."[36]

Thermo-stability means MAPs-based vaccines and medicines could reduce or eliminate cold chain requirements, which reduces cost and increases convenience and efficiency.

With certain vaccines, MAPs could be adopted despite higher costs due to these thermostability and reconstitution advantages. Yet the same study cautioned, with respect to phase 1 clinical studies for vaccines, that "a preliminary PATH cost analysis suggests the MAP presentation is likely to cost more to manufacture than the existing vaccine with needle and syringe method of both reconstitution and delivery."

The first cPAD, Uniject™, was a prefilled plastic bubble syringe with no barrel or plunger, and it launched a new era for injection technology.

This new syringe design, known as cPAD, raised hopes that safety was possible at low cost.

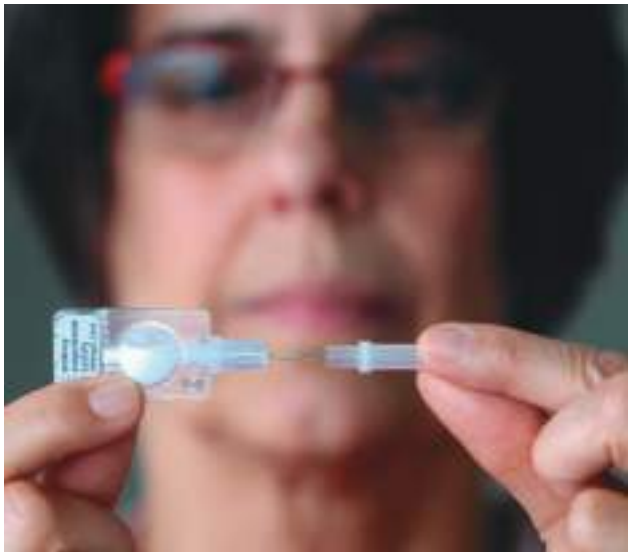
In the 1980s, the effort to develop a more affordable yet safer single-dose injection format was launched by PATH, a nonprofit global health organization, with support from U.S. Agency for International Development.

Uniject™ does not have a traditional barrel syringe and plunger. This innovative device is simple, squeeze-bubble delivery mechanism that enables almost anyone, not just professionals, to administer injections easily and safely. And, it is a prefilled single-dose device that can only be used once, eliminating contamination risk. Global immunization agencies were both impressed and hopeful that Uniject™ could lead the way toward a new era of greater coverage and safety for injections. In 2003, The Tech Museum of Innovation named PATH as that year's health category winner to highlight the originality and importance of Uniject's™ design.

PATH licensed Uniject™ to BD (Becton-Dickinson), the world's largest syringe manufacturer. 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.

Uniject™ was a format breakthrough, because it offered greater safety at a price that was competitive with single-dose vials. However, Uniject™ did not close the cost gap with 10-dose formats for per-dose delivery.

Uniject™ succeeded in opening new possibilities for injecting vaccine and medicine. But it has struggled to reach global scale due to its cost.



Uniject™ costs less than single-dose format, but more than multi-dose.

When Uniject™ first appeared it was hailed by global immunization agencies as a device that would "change the way immunization is done" and "increase…immunization substantially" in low- and medium-income nations. UNICEF's senior project manager for immunization said that the unit meant "anybody can inject…vaccine."[9]

Over the past decade or so, Uniject™ has delivered 100+ million injections of contraceptive medicine and vaccines in low- and middle-income countries. While impressive, this represents a small percentage of the billions of injections given worldwide each year. Uniject's™ scale of adoption has been limited because it costs more per dose delivered than a 10-dose vial, which remains the most popular format. As PATH noted in a 2005 overview, "As with any single-dose vaccine product, Uniject's™ single-dose format is more expensive than the multi-dose format" – although PATH also pointed out, quite correctly, many comparative cost analyses did not take Uniject's™ reduced wastage levels into account.

The problem: Uniject's™ manufacturing, filling, and sterilization processes do not create economies of scale. Instead, the device utilizes a complex, 8-step "Form-Fill-Seal" thermoset lamination method, which, combined with filling and finishing, often takes place in multiple locations over many weeks or months. Costs do not drop significantly as production volume increases.

Many other alternative vaccine and medicine administration technologies being developed require the budgets and infrastructure of high-income countries.

Not all technologies are universally suitable for use in all countries.

Vaccine and medicine delivery technologies such as pulmonary liquid aerosols and dry powders, electroporation, powder injection and mucosal vaccination face a variety of challenges.

Some are still in the very early stages of development. Other potential vaccine delivery technologies – for example, skin abrasion for transcutaneous delivery, or microporation – seem likely to require the type of manufacturing and healthcare infrastructure that is only found in high-income countries. As such, these alternative technologies are not likely candidates to solve the low-resource challenges that drive purchasing in low- and middle-income countries.

Still other technologies, such as dry powder injection, have been tried and largely left behind due to a general lack of practicality.

And, devices such as aerosol inhalers may come with the unacceptable risk (however rare or remote) of anaphylaxis or a severe allergic reaction.

Certain other technologies may require spreading their cost over many patients and frequent use, which is more readily achieved when such equipment is stocked in highly densely populated areas.

There are no "sudden surprises" in health technology. The required regulatory process is very public, and has long lead times.

Medical regulatory agencies have cautious, deliberate and methodical requirements to approve new technology.

In industries from computer software to robotics and bio-engineering, it has become almost routine for surprising new developments and revolutionary advances to appear overnight, seemingly out of nowhere, and take over an entire market.

Such rapid adoption cannot occur in health technology. Buyers, sellers, developers, users and patients always receive at least 5 years' advance notice – and often 10 years or more – that any new technology is going to enter the market, much less achieve significant scale. The reason for this years-long "Early Warning System" is the high regulatory threshold that every new medical device, drug, treatment or technology must pass before it becomes commercially available.

Getting approval for a new technology begins with a request for permission to run clinical trials, which typically takes 3 to 6 months, followed by another 3 to 6 months of institutional review board approval at the clinical site. Clinical trials themselves take several years.

In all, "Bringing a [new medical] device to market takes an average of 3 to 7 years."[37] Finally, getting through the so-called "Valley of Death" of a lengthy regulatory approval process does not guarantee that a medical device will actually achieve a market launch, much less widespread acceptance by healthcare professionals.[38]

Experience shows that cost is a key driver in the global adoption of new injection technology for vaccines and medicines.

In Low- and Middle-Income Countries, saving pennies per unit makes a difference.

In LMICs, syringe purchasing by governments is driven by extreme price sensitivity.[43] This was noted as long ago as 1999 by leading voices in WHO such as John Lloyd and Julie Milstien, who wrote:

"The margin of benefit [i.e., greater safety] is in favor of the extra cost of AD syringes, yet the price sensitivity of purchasing for the poorer countries suggests that this market will develop rapidly only when the cost is within US$ 0.02 of that of the currently available disposable syringe."[39] This extreme price sensitivity no longer controls vaccine injection purchasing in many of the world's low- and middle-income countries, because UNICEF and Gavi choose the vaccine formats for the end users. On the other hand, individual governments and private industry continue to set purchasing policies for injectable medicines and their administration technologies. Accordingly, in this sector – comprising an estimated 55 billion injections per year – cost remains a key driver in much of the world. Result: reusable syringes and glass vials prevail in these markets because they remain the lowest-cost option.

The attitude and practice in high-income countries is markedly different. Single-dose vials and single-use syringes are standard even though they cost more. Where reusable syringes are still purchased, they are usually disposed of after one use, as protocol requires.

Why does cost make such a difference for acceptance of injection technologies in low- and middle-income countries?

For countries with limited resources, it all comes down to a difficult choice.

The decades-long adoption curve for Auto-Disable syringes provides a valuable lesson on the economics of injection technology generally. Governments with constrained health resources face a painful choice.

On the one hand, if health ministries in these countries purchase safer but higher-cost devices on their fixed budgets, then they can afford to vaccinate or treat a smaller percentage of the population.

Alternatively, if these governments purchase lower-cost injection technology such as reusable syringes and 10-dose vials, they know this decision risks contamination, disease and fatalities – but they also are able to cover more of their population on a fixed budget.

Most low- and middle-income countries decide in favor of lower-cost, reusable syringes for injectable medicines.[43] They hope that "training, advocacy and regulatory factors" will reduce the incidence of syringe reuse.[40]

Regrettably, these precautionary steps often fail. According to the WHO's Lloyd and Milstien, high rates of syringe reuse (in the case of vaccines) resulted years ago from "economic necessity and cultural resistance to waste…in developing countries, regardless of training, advocacy and regulatory factors."[41]

This dynamic still applies widely when it comes to injectable medicines.

Requirements such as refrigeration, transport and sufficient numbers of trained staff all impact the practical implementation of injection technology.

Contributing to the total cost per dose delivered are "hidden" factors such as overfill, wastage, cold chain storage, breakage and time demands on health workers. All have implications for injection technology design.

Vaccines and medicines are not always administered in ideal environments.

Refrigerated storage with 24/7 monitoring and emergency power supply can be limited in some zones, especially if unrefrigerated trucks transport medicine or vaccine over the "last mile." Costly insulated boxes with cold packs may be required.

The impact on injection technology is to put a premium on efficient cold chain storage (small space requirements per dose).

Transportation alone can increase costs. For example, when glass vials break in transit, the contents must be replaced, placing an economic premium on minimizing or eliminating the use of glass.

The availability (or lack) of trained staff also affects the real-world efficiency of injection technologies. As *Plotkin's* reports, ordinary needle and syringe injection "requires highly skilled staff," and more complex injection processes require more highly skilled staff. "The lack of enough skilled administrators to inject vaccines is a global problem," stated this source."[42]

The impact on injection technology is to put a premium on formats that are simple to administer.

The planned ApiJect Prefilled Injector is designed for both economic efficiency and accessibility.

The ApiJect Prefilled Injector* is planned to combine the globally-trusted technologies of Blow-Fill-Seal and pen needle-style hubs, supporting safety, quality and low total cost.

In compliance with the Target Product Profile for cPADs developed by PATH, ApiJect Systems, Corp. is has designed a prefilled single-dose delivery system. The ApiJect Prefilled Injector's new modular format could potentially provide greater economic efficiency than the 10-dose vial.

ApiJect will seek to reduce the need for the use of glass vials for drug distribution, as well their use as containers for syringe filling by medical staff prior to final injection. The ApiJect Prefilled Injector is engineered to deliver all the benefits of a cPAD like Uniject™, combined with economic efficiency. The injector's total cost per dose delivered will potentially be aligned with that of a 10-dose vial and 10 syringes. Savings could potentially come from efficiencies in manufacturing, transport, labor and low waste.

Because the ApiJect System plans to utilize Blow-Fill-Seal technology (BFS), its manufacturing costs are in line with those of a 10-dose vial. Less overfill for prefilled formats also supports economic efficiency. In addition, ApiJect will seek to realize potential cost reductions at every step from initial orders through final delivery. In-market levels of wastage of medicine and vaccine is the biggest hidden factor in the actual "total cost" of biologicals delivered in 10-dose glass vials. Single-dose potentially reduces waste, while plastic construction could potentially address the high cost (and high energy use) of glass manufacturing and container breakage during shipping or in the field.

*Products shown for informational purposes only, not for use in product promotion.
ApiJect's Prefilled Injector and other products have not been reviewed or cleared by FDA or other regulatory authorities for distribution.

The planned ApiJect Prefilled Injector* is designed to potentially achieve quality, scale and affordability through the use of Blow-Fill-Seal technology.

BFS is a trusted sterile process for aseptically filling drugs.

Blow-Fill-Seal (BFS) manufacturing has been accepted by regulatory agencies for global use. Some 50 billion sterile BFS containers per year are produced for eye drops, ear drops, nose sprays and (in ampoules) certain retrovirus vaccines.

BFS is a high-efficiency, low-heat, low-cost manufacturing method. A single machine forms, fills, sterilizes and seals the container in a matter of seconds. Each unit is filled with vaccine or medicine, within a sterile area of the manufacturing machine, as part of production. No extra steps for filling, sterilizing and finishing are required.

Subject to regulatory approval, ApiJect plans to utilize BFS technology to manufacture a plastic container that is married with a prefabricated Needle Hub.*

The current generation of BFS machines has the capacity to produce up to 25,000 finished devices per machine, per hour.

Again, subject to regulatory approval, each ApiJect device is planned to be filled with vaccine or medicine within a sterile area of the manufacturing machine, as part of production. No extra steps for filling, sterilizing and finishing of the ApiJect device would be required.

The entire BFS process – manufacturing, filling, sterilizing and sealing – takes 3 to 15 seconds per unit – start to finish.

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The planned ApiJect Prefilled Injector* is intended to provide economic efficiency without compromising patient safety, supporting worldwide adoption.

New injection technology needs to be simple, easy to use and affordable.

For 30 years the global health community has sought a more-economical alternative to the 10-dose vial that could deliver all the advantages of prefilled formats.

These advantages include: automatic precision dosing because containers are machine-filled; greater safety because cross-contamination is virtually eliminated; less waste of leftover vaccine in open vials; and lower costs which can enable healthcare organizations to vaccinate more people with identical budgets.

ApiJect's injector* is planned as a disposable, single-dose cPAD format, with cost factors that can potentially put a prefilled single-dose injector within reach, even for resource-challenged care providers.

Economic efficiency potentially contributes to extensive coverage by enabling existing healthcare budgets to fund additional vaccinations for the same dollars.

Safety is supported because prefilling means there is no chance of vial contamination. In addition, the device is designed with Auto-Disable features, intended to make reuse difficult and thereby potentially combat the spread of disease through contamination.

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After 165 years of traditional syringes and glass vials, injection technology is moving toward a historic shift. Cost considerations, safety, scalability and ease of use will remain critical factors, as will regulatory approval.

The 30 "Soft Benefits" that a BFS Prefilled Syringe Could Provide to Improve Lives in All Markets

A single-use, compact, BFS prefilled syringe could offer dozens of meaningful real-world, quality-of-life improvements for patients around the world.

A BFS prefilled syringe could be designed to provide the quality, safety, and convenience of a prefilled syringe with the scalability and cost of multi-dose formats.

1 Coverage and Equity

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

More than 3 million people die from vaccine-preventable diseases each year. Of these deaths, approximately 1.5 million are in children less than 5 years old.[1] And vaccines represent just 10% of greater injection access to other medicines as well would be game-changing.

To address these essential health services worldwide, it is estimated that there are approximately 7.2 million health workers in total.[2] This includes doctors and nurses, but also community health workers (CHWs).

Even with an estimated 1.3 million CHWs in the world today,[3] there is still a severe shortage of healthcare workers, leaving communities vulnerable to death and disease. If CHWs were empowered with tools such as BFS prefilled syringes that were adaptable to rural and fragile settings, they could help fill the gaps in access to care.

As Dr. Henry Perry, senior scientist at Johns Hopkins Bloomberg School of Public Health, stated: "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."[4]

2 CHW Empowerment

With government approval, an easy-to-use prefilled syringe could potentially enable millions of community health workers (CHWs) and midwives to give injections.

A BFS prefilled syringe could be designed to be intuitive and easy to administer, requiring minimal training.

Whether a single unit or quickly assembled from simple components by the CHW onsite, the BFS prefilled syringe needs to be compact and reliably make it to the final destination ready for immediate use by the health worker.

Once activated, the needle cannot be detached and the device cannot be refilled – making it a compact Prefilled Auto-disable Device (cPAD).

The ease of the system should allow CHWs to provide injections to people who live far from clinics and would otherwise go without.

3 Self-Injection Option

An easy-to-use BFS prefilled syringe would potentially enable patients to self-inject with success and confidence, where appropriate and approved (e.g., contraceptives).

Family planning is not only fundamental to the well-being and autonomy of women, but also to the health and development of communities.[5] And, when women and adolescent girls have access to a variety of contraceptives, they are more likely to find and use a method that meets their needs and preferences.[6]

Self-injectable contraceptives have the potential to be that option as they are highly effective, safe, and private, as well as able to increase access and empower women to manage their reproductive health.[7]

This is confirmed by the World Health Organization (WHO) supporting self-injection where women have access to training and support.[8]

The option of self-injection can be applied to other drugs and vaccines, in addition to contraceptives. A BFS prefilled syringe needs to be able to meet a variety of patient needs for those who would choose self-injection for convenience or other preferences.

4 Labor Utilization

More time can be spent helping patients if community health workers do not have to fill syringes from vials.

Traditional glass vials and the accompanying syringes are labor-intensive.

They require preparing fresh needles and syringes for each patient, checking to ensure that the right vial with the correct vaccine or drug is ready for use, inserting the needle into the vial, withdrawing the proper dose and checking it. In busy clinics, time that could be spent treating more patients or spending longer with each patient, must instead be spent on these steps. Furthermore, more errors can occur with these multiple steps.

A BFS prefilled syringe could be designed so that there is no need for withdrawal from a vial; no checking of proper dosage; and no preparation of fresh needles and syringes for each patient.

A BFS Prefilled Syringe could allow the healthcare professional to just activate the device (and assemble if required), remove the protective needle cap, and administer the injection... then discard the unit and get ready for the next patient.

5 Injection Process Efficiency

One important benefit of a BFS prefilled syringe would be more efficient injection administration, allowing for higher volume of patient throughput.

Prefilled formats allow healthcare professionals to inject more patients in less time, especially in mass vaccination settings. This is especially important when time is limited in crisis situations.

Using traditional glass vials to vaccinate requires nurses' and health providers' valuable time; this is not ideal in a crisis situation where large numbers of people need interventions quickly. The exact amount of medicine needs to be measured and withdrawn from each vial, using a separate syringe to withdraw than to inject the vaccine or medicine.

A 2014 time and motion study conducted by PATH indicated that dispensing vaccine from a 10-dose vial takes exactly twice as long per injection as dispensing vaccine from a prefilled single-dose device (in this case, Uniject™).

The difference: on average, it took healthcare workers 15.2 seconds to give an injection from a 10-dose vial. It took 7.6 seconds on average for health workers to give an injection from the prefilled device.[9]

6 Dosage Accuracy

Precision prefilling of a BFS injection system can potentially increase confidence and efficacy of delivering correct results.

Healthcare professionals must withdraw precisely the correct amount of vaccine or medicine from a multi-dose vial to fill the syringe for each injection.

This requires knowledge and skill. Without this training to properly administer injections, it's easy to under-dose or over-dose a patient.

Health workers are particularly vulnerable to making mistakes with injections because they often work long hours, under considerable stress, and are frequently interrupted in the process of preparing or administering injections.

According to an advisory from the Patient Safety Network of the U.S. Department of Health and Human Services (most recently updated in September of 2019), "A review of 36 studies on caregiver medication errors found error rates ranging from 2%–33%, with dosage errors, omissions, and wrong medication the most common types of administration errors."[40]

Automated prefilling of a BFS injection system at the time of manufacturing would eliminate the need to withdraw liquid from a vial, potentially reducing over- and under-dosing, and enhancing patient safety by eliminating the use of vials, the possibility of vial contamination is also eliminated.

7 Intradermal/Subcutaneous Needle Opportunity

Prefilling does not require fluid withdrawal from a glass vial using long needles. A BFS prefilled syringe could be designed to support ID and SC needle lengths.

Needles and syringes limit accessibility to needed medicines and vaccines by requiring a trained medical professional to administer them in clinical settings…and in many parts of the world, trained professionals are not always available.

A BFS prefilled syringe affixed with a short ID needle could allow for an intradermal injection that followed the same procedure as if it were an intramuscular injection.

With regulatory approval of a BFS prefilled syringe with an ID needle, many patients could potentially self-inject, reducing the need for healthcare workers and eliminating the need to prepare a needle and syringe.[10]

In a world where there is a shortage of healthcare workers, this is life-changing for millions of people, including an estimated 214 million women in developing countries who would like to delay or prevent pregnancy but are not using any method of contraception.[11]

Replacing glass vials and syringes has the potential to transform the way people access and receive medicines and vaccines in low-resource, non-clinic settings.

8 Reliable Aseptic Filling

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

Around the world, BFS technology is currently used to reliably and aseptically manufacture, fill and finish 50 billion low-cost plastic containers every year.

Contents include sterile eyedrops, eardrops and nasal sprays as well as a limited number of oral vaccines.[41]

Using a low-heat process, BFS technology can safely package most liquid biologicals, including vaccines that are suitable for medical countermeasures.

Based on past experience with biologicals in (non-injectable) BFS formats, the result could potentially be a Prefilled Injector* with a validated shelf life of 2-3 years. In some cases,10-year shelf life may be possible.

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."[42]

 ApiJect's products have not been cleared by the FDA or other regulatory authorities for distribution.

9 Fractional Dose Option Conserves Vaccine Supply

In situations where certain vaccines are in short supply, administration of fractional ID doses increases coverage and the number of lives saved.

Some vaccines, if delivered intradermally, would only require 1/5 of a 0.5ml dose of a vaccine or medicine, with the same efficacy.

This would enable the vaccination of five times as many individuals using the same amount of vaccine, which could be game-changing in situations where there is a limited supply of vaccines or medicines – particularly if there is a significant risk of disease or outbreak.

Using ID delivery methods in these cases of vaccine shortage could increase immunization coverage, while decreasing costs or holding them steady, and maintaining the same immune response and safety. A BFS prefilled syringe designed to be affixed with an ID needle would only need to be filled with fractional doses, potentially enabling the device to meet these needs and administer vaccines more broadly with at least comparable quality and protection.

10 Lower Needlestick Risk

Less handling and fewer steps involved could reduce the chance of accidental needlestick of both the patient and the person administering the injection.

Healthcare workers are always at risk for needlesticks when handling syringes that accompany glass vials, both when using them on patients and when disposing of them.

This risk is often greater in areas where the ratio of healthcare workers to population needs and disease burden is small.[12] Healthcare workers are often hurried with many patients to see and few staff, increasing the probability of needlesticks in these environments. A BFS prefilled syringe should require fewer steps to administer an injection and, therefore, takes less handling by healthcare workers. This potentially results in fewer opportunities for needlesticks.

This risk of needlesticks and, therefore, possible infection further demonstrates that unsafe injections are dangerous not only for recipients, but for those delivering the necessary medicine or vaccine.[13]

11 A Single-Dose Unit for One-Time Use

A BFS prefilled syringe could be designed to prevent reuse, potentially reducing the spread of disease through a future design with additional auto-disable features.

Up to 70% of injections are given with reused syringes and needles in some low- and middle-income countries[14] and unsafe injections annually result in 15 million Hepatitis B infections (25% of new cases), 1 million Hepatitis C infections (8% of new cases), and 340,000 HIV/AIDS infections (5 – 14% of new cases).[15] Improper reuse is also an issue in high-income countries. A 2010 survey of 5,446 U.S. healthcare professionals revealed how these infections can happen:[16]

- Nearly 1% of respondents acknowledged that they sometimes or always reused a syringe for more than one patient after changing only the needle.
- 6% of respondents admitted to sometimes or always using single-dose or single-use vials for multiple patients.
- 15% of respondents reported using the same syringe to re-enter a multiple-dose vial numerous times. Of this group, about 7% reported saving these multiple-dose vials for use with other patients.

Glass vials and syringes leave the door open for unsafe injection practices, resulting in more than one million deaths a year. Since a BFS prefilled syringe would be prefilled at the time of manufacturing, it eliminates the need to withdraw liquid from a vial and, therefore, the possibility of vial contamination.

12 No Risk of Glass Flaking Contamination

Using a device made of medical-grade plastic eliminates contamination of medicine from glass flaking.

When top layers of a glass surface separate and flake off, this results in glass flaking or delamination.

When the flakes, often not visible to the human eye, mix with the vial contents, the result is dangerous contamination. Flaking is common in glass vials and occurs when chemicals from the product or the manufacturing process cause the glass surface of the vial to delaminate or discolor.[17]

This can happen at any point during the vial's life: manufacturing, heat treatment, sterilization, or stability testing, making it especially difficult to identify, and especially dangerous.[18]

Delamination reduces a drug's safety and efficacy, and poses a serious contamination risk to any patient who receives an injection of the vial's contents.

A BFS prefilled syringe can eliminate this risk, helping to improve patient safety.

13 Reduced Drug Waste

A single-dose prefilled format, such as a BFS prefilled syringe, should result in less drug product being discarded than multi-dose formats because it typically has lower overfill rates, and a reduced likelihood of unused drug product expiring.

When multi-dose vials of vaccine are opened for use, if there is any leftover vaccine at the end of an injection session, then the leftover vaccine is stored in a refrigerator and a countdown begins for its expiration. For lyophilized vaccines, expiration occurs within hours and drives wastage rates that can run from 20% to 60%.[19]

Liquid vaccines (non-lyophilized) have a longer shelf life before they expire – 28 days in most cases – but their expiration date remains a significant cost factor. Liquid vaccines' 28-day expiration can result in double-digit percentages of vial content being wasted.[20] Numerous studies published by PATH and reports from the WHO show wastage rates for 10-dose vials typically range from 20% to 40%.[43]

Single-dose formats eliminate the waste of vaccines and drugs that occurs when multi-dose vials are opened and "leftover" drug substance expires before it can be used.

14 Drone Delivery Option

Because a BFS prefilled syringe would be made primarily of pharmaceutical-grade plastic, doses in this format can potentially be more safely airdropped with less need for special packaging and less risk of breakage.

A BFS prefilled syringe would feature lightweight and durable construction, potentially enabling it to be delivered through increasingly effective non-traditional distribution methods, such as drones.

This is particularly useful in environments where vaccines or medicines have difficulty reaching the last mile.

A BFS prefilled syringe's composition of flexible and resilient plastic could make it a much more versatile delivery method, potentially providing more transport options and facilitating increased access to the vaccines and medicines so desperately needed.

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 a small vehicle, or by drones.

Excluding vaccine cost, the cost for transportation and cold chain storage is the greatest contributor to the Total Cost of Delivery for vaccines.[21]

Glass is expensive to produce as it is highly energy-intensive, and it is heavy to transport, particularly to the kinds of remote locations most in need of vaccines and medicines.

The polymer format of a BFS prefilled syringe potentially makes it possible to carry more doses greater distances, reaching more people in need of vaccines and medicines with less cost and effort.

16 Simplified Training

A BFS prefilled syringe would not require careful filling from a vial or aspiration. Nor would it require precision dosing by the administrator, or pushing down on a plunger to give an injection. This comparative ease of use could make the device a potential candidate for home administration or self-administration, with relatively brief training.

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).[22]

A BFS prefilled syringe should require significantly fewer steps to prepare and administer an injection, perhaps as few as half the steps needed for traditional formats, depending on human factors studies by market.

Nearly any adult or teen can potentially become competent with it following brief training, in some cases perhaps in a single session.

If patients had the ability (and regulatory permission) to inject themselves or if healthcare workers could inject patients in non-clinical settings because traditional syringes and vials weren't necessary, it would ensure coverage of many more people in need of life-saving medicines and vaccines.

17 Less Overfill

Prefilled syringes typically require only 5% overfill of antigen compared to the standard 20% overfill per multidose vial – potentially reducing wastage.

10-dose vials incur higher vaccine costs than single-dose vials or syringes due to a regulatory requirement of a 20% "overfill" ratio.[23]

Pharma suppliers must put more vaccine into each vial than just the amount needed for 10 doses.

This is done in order to compensate for any liquid vaccine that may be lost or become inaccessible (at the bottom of the vial, etc.) while a health worker is withdrawing a dose or injecting a patient – neither of which is a totally efficient process.

A precisely prefilled single-dose injector such as a BFS prefilled syringe can potentially achieve significant waste reduction.

18 Pandemic Response Time

Ramping up to high-volume production can potentially be accelerated with the Blow-Fill-Seal drug packaging process.

A single BFS production line can aseptically manufacture, fill and finish 15+ million single-dose units of a vaccine or drug per month, with a week or less of lead-time.

Manufacturing lead-time for glass results in a slow crisis response.

For glass, the traditional aseptic filling process can take up to 12 steps, involves numerous people, and may require months to complete.[24] Raw materials requirements and manufacturing processes mean that glass vials must be ordered up to 6 months or more in advance, which is too slow to address mass outbreaks or crisis situations.

The potential for BFS plastics technology to begin supplying medicines or vaccines in prefilled containers on short notice (1-2 months) at population scale is due to its simplified manufacturing process.

19 Patient Adherence

Because a BFS prefilled syringe can be designed to be convenient, easy to use, and discreet, patients are potentially more likely to stay with longer-term treatment regimens such as TB, allergy injections, HIV, contraception, etc.

Adhering to a medical protocol can be challenged by many factors, such as cost and distance to a clinic, and can result in patients not getting their injections.

Self-injection (when approved at the option of regulatory authorities) can address some of those issues. For example, the ability to self-inject contraceptives can encourage continuation of contraceptive coverage as it addresses some of the reasons why women discontinue use, such as travel expenses and long distances to the clinic, and long waits at the clinic.[25]

For young women and adolescents, who often have higher rates of contraceptive discontinuation, and who also place a high value on their privacy, self-injection can offer independent and discreet contraception use over a longer period of time.[26]

A BFS prefilled syringe could potentially support and increase in the number of patients who will remain current on longer-term courses of treatment.

20 Surge Pandemic Coverage

A faster manufacturing format designed for simplicity and ease of use at the point of care can potentially support faster, wider vaccinations of more people, by more people.

A BFS prefilled syringe can be designed for ease of use and quick training, potentially enabling more healthcare workers, including crucial CHWs, to help vaccinate large numbers of people needing interventions.

Additionally, its small, lightweight, easily transportable format could potentially support healthcare professionals as they seek to reach more people, which is crucial when an entire population requires emergency vaccination.

The single-use format of a BFS prefilled syringe can potentially reduce these risks, especially if designed with an auto-disable feature to ensure that the device cannot be used again.

In a national emergency where authorities are arranging for mass vaccinations, a BFS prefilled syringe could potentially achieve population-scale production on an accelerated basis, making it possible to address the urgent need of many more people, much more quickly than present capacity.

21 Last Mile Transportability

A smaller, lighter, high-density format is more compact and thus potentially easier to deploy for local field operators.

A BFS prefilled syringe could be designed for portability and robust usability, making it potentially suitable for field operations in remote areas or rugged terrain.

The lightweight plastic format will not require a separate syringe, or two separate syringes in the case of needing to add an adjuvant to a vaccine, or in case of needing to withdraw the liquid from a vial and then inject it with a shorter syringe.

Its compact design would make the BFS prefilled syringe relatively easy to carry into the field far distances and to many different locations, and for health workers to manage as they deliver vaccines and medicines.

22 Anti-Counterfeiting

As opposed to vials and syringes, which are commodities, BFS prefilled syringes would be harder to duplicate and package counterfeit drugs in, potentially helping to reduce drug counterfeiting.

The World Health Organization (WHO) estimates that 10% of the global market for pharmaceuticals is comprised of counterfeits; the percentage of phony products can be as high as 50-70% in developing countries according to some.[27] Drugs counterfeited included antibiotics, hormones, analgesics, steroids, and antihistamines, and can be grouped into six categories: (1) Products without active ingredients, 32.1%; (2) Products with incorrect quantities of active ingredients, 20.2%; (3) Products with wrong ingredients, 21.4%, (4) Products with correct quantities of active ingredients but with fake packaging, 15.6%; (5) Copies of an original product, 1%; and (6) Products with high levels of impurities and contaminants, 8.5%.[28]

Counterfeit drugs result in an annual death toll of approximately 1 million, according to the WHO.[29]

As the BFS process requires significant capital expenditure upfront to set up and cannot be purchased as empty containers ready to be filled, a BFS prefilled syringe will be significantly harder to pass counterfeit drugs in, potentially improving patient safety in that market.

23 Small Manufacturing Footprint

BFS technology is small and efficient. A $7M machine capable of delivering up to 180 million doses a year fits in a shipping container and can be set up in any suitable location.

Blow-Fill-Seal (BFS) is a proven, reliable, 70-year-old drug packaging technology.

Each year, some 50 billion BFS containers are aseptically filled with sterile eyedrops, nasal sprays, and ear drops. BFS manufacturing is a high-efficiency, low-heat, economically efficient process that is radically simpler and faster than glass manufacturing.

There are no extra steps required for filling, sterilizing, and finishing of a BFS prefilled syringe. Plastic resin is melted by an extruder at high temperature and pressure, forming a molten plastic tube.

The tube is cooled and filled with liquid medication in a sterile area inside of the manufacturing machine, and then sealed. The entire BFS process – manufacturing, filling, sterilizing, and sealing – takes 3 to 15 seconds per unit – start to finish.

The current generation of high-end BFS machines has the capacity to aseptically package up to 25,000 doses per hour.[30]

24 Pocket Portable

A BFS Prefilled Syringe can be designed to be small, light, and sturdy – enabling it to be carried in a pocket without breaking.

The BFS Container for a BFS prefilled syringe can be designed to be only a couple inches long (less than 10cm) and made of soft, sterile, pharmaceutical-grade low-density polyethylene (LDPE). And the Needle Hub could be made of light but durable polypropylene (PP), plus the needle.

Its weight and compact size would enable it to be easily transported long distances to clinics on foot, bicycle, or other modes of transportation.

In addition, its plastic construction is designed to make the unit robust and durable enough to be carried in a pocket, medical bag, or any container with minimal risk of breakage.

25 Animal Use Version

A version of a BFS prefilled syringe can be designed for use with critical small animal needs, especially in areas with low veterinary coverage.

When treating a sick animal, it is imperative that the proper dose of medicine is used, as too much of the drug can kill an animal, while too little won't cure the disease ailing the animal.[31]

Reducing the steps required for an injection (and, therefore, the time it takes to give an injection) potentially makes it easier for the person administering the injection, and can also make the injection process less stressful for the animal needing human assistance.

If a prefilled single-dose unit such as a BFS prefilled syringe were available to farmers and veterinarians – approved at the option of regulatory authorities – there potentially could be wider coverage, reducing the number of animals that otherwise would go unvaccinated or untreated.

26 Environment: Energy and Materials

BFS prefilled syringes should be designed to use less energy and raw materials in manufacturing than glass.

The industrial sector, encompassing manufacturing, mining, agriculture, and construction, accounted for nearly a third of total U.S. energy use in 2012.

Of those industries, manufacturing, which includes the glass industry, accounted for a little more than half of total industrial energy use.

Glass manufacturing is one of the economy's most energy intensive industries.[32] The bulk of energy consumed in the glass manufacturing industry comes from natural gas combustion used to heat furnaces that melt raw materials and form glass (most furnaces are natural gas-fired, but there are a small number that are electrically powered).

Furnaces used to melt raw materials into glass need to burn 24/7, using a great deal of energy at a consistent rate.

Many glass furnaces also use electric boosting or supplementary electric heating systems to increase throughput and quality.[33]

27 Environment: Disposal Waste

A BFS prefilled syringe should be designed with very few components and mass, potentially resulting in less waste after the device is used.[44]

With BFS plastic syringes, there would be no need to dispose of bottles, stoppers, crimps, and various other components used to make traditional vials and syringes.

The volume of raw materials that would be used in each BFS prefilled syringe could be designed to be relatively low compared to other formats. This factor also contributes to less disposal waste.

28 Environment: Manufacturing Process Pollution

Plastic manufacturing results in relatively low environmental pollution and has a smaller carbon footprint, compared to other typical container materials, according to recent studies.[45]

Manufacturing glass vials causes water pollution, uses non-renewable raw materials, such as sand and minerals, and produces waste from the by-products of those necessary raw materials, as well as the glass itself.[34] [35]

In fact, producing a ton of glass from raw materials creates 384 pounds of mining waste.

Additionally the combustion of natural gas and the decomposition of the raw materials that form glass during the melting process lead to the emission of CO_2.[36]

29 Compact, Reliable Supply Chain

Compared to the supply chain required to support glass vials, BFS prefilled syringes should only require two raw materials and the entire fill-finish process can be done in two facilities.

A BFS Prefilled Syringe should require only two raw materials: pharmaceutical-grade polymer resin (i.e. plastic) and hypodermic needles. Both products should be easy to source in major markets.

Manufacturing a BFS prefilled syringe should be feasible in two facilities. The first facility would create the Needle Hub and its Connector that affixes it to the BFS Container. This facility would produce all of the plastic-injection molding parts and assemble them, along with the hypodermic needle, into the two aforementioned components.

The second facility would be where the BFS manufacturing line is held. There, the drug product would be filled into a BFS Container, quality tested, and then finished for transportation.

If the BFS prefilled syringe were meant to arrive at its final destination pre-assembled, the attachment of the Needle Hub and Connector to the BFS Container could also be done in the BFS facility just prior to secondary packaging.

This compact and reliable supply chain could potentially minimize the risk that the final device with the drug product do not arrive at their final destination.

30 No Glass to Break

A BFS prefilled syringe would not use any glass. The result would be potentially less breakage in manufacturing or transit, resulting in reduced cost and wastage.

Traditional vials are also subject to costly recalls from flaking or other issues; and syringes too can be recalled.

Over the past five years, more than 20 product recalls have been associated with glass issues, and over 100 million units of drugs packaged in vials or syringes have been withdrawn from the market.[37]

In the 10 years prior, approximately two million glass vial and syringe units were recalled.[38] Additionally, nine warning letters citing glass-related problems were issued in the past five years, and seven during the decade before.[39]

These limitations of glass packaging cost companies millions of dollars in lost revenue, but the industry is reluctant to adopt new technologies due to the cost of switching formats.

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A BFS Prefilled Syringe Offers 30 "Soft Benefits" that

The benefits of a BFS prefilled syringe cannot be assigned a specific dollar

1. Coverage and equity
Could improve delivery of injectable medicines and vaccines to 400+ million patients in remote places, far from medical staff and clinics.

2. CHW empowerment
Millions of community health workers and midwives – with governmental approval – could give injections because of the ease of the process.

3. Self-injection option
Patients could self-inject with success and confidence, where appropriate and approved (e.g., contraceptives).

4. Labor utilization
No time would be spent filling syringes from vials – allowing more time to help patients.

5. Injection speed
Health workers could inject more patients in less time, especially in mass inoculation settings. This is especially important when time is limited in crisis situations.

6. Dosage accuracy
A BFS machine would perfectly fill a BFS prefilled syringe every time, eliminating the chance of over- or under-fill.

7. Intradermal/subcutaneous needle optionality
Prefilling would not require fluid withdrawal from a glass vial using long needles. A BFS prefilled syringe would supports even the shortest ID needle.

8. Reliable aseptic filling
BFS technology is accepted by the FDA and regulatory health agencies worldwide.

9. Fractional dose option conserves vaccine supply
In situations where certain vaccines are in short supply, administration of fractional ID doses increases coverage and the number of lives saved.

10. Lower needlestick risk
Smaller format would reduce chances of accidental needle-stick for both the patient and the administrator.

11. Designed for one-time use
Single-use feature would prevent reuse, reducing spread of disease.

12. No risk of glass flaking contamination
Medical-grade plastic would eliminate contamination of medicine from glass flaking and thus no glass-based recalls.

13. Reduced drug waste
Single-dose, prefilled syringe could avoid "extra" medicine being thrown away unused or expired. Especially valuable in countries with high volumes of 10-dose glass vials.

14. Drone delivery option
Doses could potentially be safely air dropped 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.

are Difficult to Measure, but Improve Lives in Many Ways

– but they still provide meaningful real-world quality-of-life improvements

16. Simplified training
A BFS prefilled syringe would not require anyone to learn how to precisely fill the correct-sized dose from a vial, or how to push down on a plunger to give an injection. This could reduce the number of steps for preparation and administration.

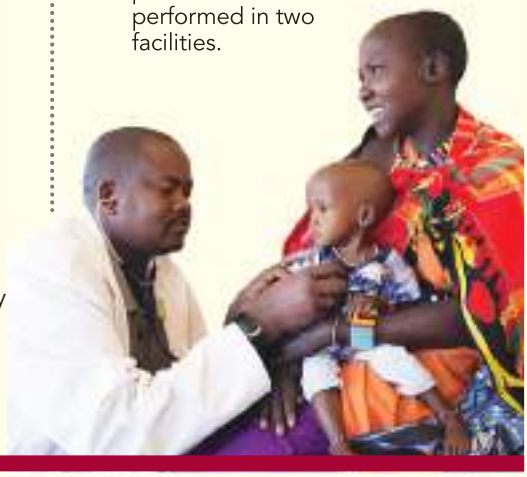
17. Less overfill
Precise prefilling requires less overfill of antigen per dose than the normal 10% per vial.

22. Anti-counterfeiting
BFS prefilled syringes would be harder for counterfeiters to duplicate.

23. Small mfg. footprint
BFS technology is small and efficient. A $5M machine capable of delivering up to 25 million doses a year fits in a shipping container and could be set up in any suitable location.

24. Pocket portable
Would be sufficiently small, light and sturdy – able to be carried in a pocket without breaking.

28. Supply chain
A BFS prefilled syringe could be designed to require only two raw materials, and the fill-finish process could be performed in two facilities.



18. Pandemic response time
Surge production would be much faster than glass vials and could get large quantities of an antidote from factory to the public in days or weeks.

19. Adherence
Simpler format means patients would be more likely to stay with longer term treatment regimens such as TB, allergy injections, HIV, etc.

20. Pandemic coverage
Would allow faster, wider inoculations of more people, by more people.

21. Transportability
A smaller, lighter, high-density plastic format would be more compact and thus easier to deploy for local field operators.

25. Animal use version
Could be designed for small animal needs, especially in areas with low veterinary coverage.

26. Environmental impact: energy and materials
Should use less energy & raw materials in manufacturing.

27. Environmental impact: disposal waste
Would potential create less waste after device is used.

29. Environmental impact: manufacturing pollution
BFS manufacturing results in relatively low enviromental pollution and has a smaller carbon footprint, compared to the process employed for other typical container materials.

30. No glass to break
Zero glass breakage in manufacturing or transit. Less cost. More coverage.

ApiJect's products have not been cleared by the FDA or other regulatory authorities for distribution.

ApiLabs

Injectable Contraceptives Improve the Health and Lives of Women – and Transform Communities

Lack of access to family planning resources affects the lives of millions of women around the globe, causing unnecessary and untimely deaths. Injectable contraceptives are a highly effective intervention and empower women to manage their reproductive health.

Millions of women lack access to family planning, despite wanting to delay or prevent pregnancy. This results in avoidable maternal and newborn deaths, and poor outcomes for women and children.

Making injectable contraceptives available to every woman who wants access to them can alter communities, strengthen economies, and save lives.

Family planning is one of the most crucial interventions that improves the health of women, children, and communities.

Family planning not only affects health, but improves outcomes at the community level.

Family planning is one of the most fundamental interventions that has a direct impact on women and their long-term health. It allows spacing of pregnancies, prevents unintended pregnancies, limits the number of pregnancies, and delays pregnancies in young women who are at an increased risk of health problems and death from early childbearing.[1]

Babies born too closely together or pregnancies that occur too quickly after a previous pregnancy contribute to some of the world's highest infant mortality rates.[2] Additionally, infants whose mothers die from childbirth have a greater risk of ill health and death.[3] Neonatal mortality is higher for adolescent mothers, who are also more likely to give birth to babies with a low birth weight or babies born prematurely.[4] Family planning enables women to choose when and if they become pregnant in the first place.[5] It gives them power and autonomy over their sexual and reproductive health and allows them to make informed decisions.

It also unlocks other potential opportunities in life for women. They can consider other endeavors, such as a career or education, which not only enhance women's lives, but fuel economic growth. Family planning provides more opportunities for children as well, including adolescent mothers.

According to WHO, adolescent mothers find it easier to keep attending school while raising fewer children, and children with fewer siblings typically remain in school longer, suggesting that contraceptive use improves educational outcomes for both mothers and children.[6]

Millions of women still don't have access to family planning. This inequity results in unnecessary health risks and deaths every day.

Women face many obstacles to family planning across the world.

Many women around the world lack access to modern contraceptive methods or rely on methods controlled by men. The absence of options for preventing pregnancy leads to many maternal and infant deaths.

In developing regions, some 214 million women who want to avoid pregnancy are not using safe and effective family planning methods, for many reasons, including:[7]

- Limited choice of methods
- Limited access to contraception, particularly among young people, poorer segments of populations, or unmarried people
- Fear or experience of side-effects
- Cultural or religious opposition
- Poor quality of available services
- Users' and providers' bias
- Gender-based barriers

This is a crucial problem as family planning is not only fundamental to the well-being and autonomy of women, but also to the health and development of communities.[8] It saves lives of mothers and children.

Growing populations and a shortage of family planning services contribute to a lack of access.[9]

- In Africa, 24.2% of women of reproductive age have an unmet need for modern contraception.[10]
- In Asia, and Latin America and the Caribbean – regions with relatively high contraceptive prevalence – unmet needs are 10.2 % and 10.7%, respectively (Trends in Contraception Worldwide 2015, UNDESA).[11]

Regions where contraceptive options are limited often lack access to basic maternal healthcare as well, making unplanned pregnancies even more dangerous.

Adequate family planning helps women manage their reproduction, providing a more favorable outcome for them and their children.

Lack of access to family planning options – especially access to contraceptive methods that women can select and administer on their own initiative – results in women being more likely to die from pregnancy and childbirth complications.[12]

Where contraceptive options are limited or non-existent, access to healthcare can also be scarce. Thus, unplanned pregnancies can result in deliveries unattended by healthcare workers.

Almost all maternal deaths (99%) occur in Low- and Middle-Income Countries (LMICs), where access to healthcare workers can be limited.[13] Some 60% of women in LMICs give birth with no medical professional present, and as a result, approximately 800 mothers a day die from hemorrhage, while additional maternal lives are lost due to eclampsia, problematic labor and other reasons.

In 2012, an estimated 80 million women in developing countries had an unintended pregnancy.[14] Unplanned pregnancies can also lead to unsafe abortions, which account for between 5 and 13 per cent of all maternal deaths.[15] Investing in family planning not only saves lives, but can also improve lives. According to the Gates Foundation, every dollar spent on family planning has the potential to save governments up to 6 dollars that can then be used on other public services, such as health, housing, water, and sanitation.[16]

Many maternal deaths are avoidable with greater access to family planning resources and by empowering women to have control over their family planning needs.

Putting reproductive choices in the hands of women through interventions such as contraceptives changes the outcomes for millions of women.

Maternal deaths can be significantly reduced or avoided by delaying motherhood, spacing births, preventing unintended pregnancy, and avoiding unsafely performed abortions. One way to address these challenges is through contraceptives. "Contraceptives are highly cost-effective health investments which save lives. If every girl and woman who wanted to use modern contraception was able to, we could prevent 170,000 maternal deaths and around 1.6 million newborn deaths each year" said Alvaro Bermejo, Executive Director at the Children's Investment Fund Foundation.[17]

And when women and adolescent girls have access to a variety of contraceptives, they are more likely to find and use a method that meets their needs and preferences.[18]

Contraceptive use has increased in many parts of the world, especially in Asia and Latin America, but continues to be low in sub-Saharan Africa. Globally, use of modern contraception has risen slightly, from 54% in 1990 to 57.4% in 2015.

Regionally, the proportion of women aged 15–49 reporting use of a modern contraceptive method has risen minimally or plateaued between 2008 and 2015. In Africa it went from 23.6% to 28.5%, in Asia it has risen slightly from 60.9% to 61.8%, and in Latin America and the Caribbean it has remained stable at 66.7%.[19]

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 (where permitted at the option of regulatory authorities), more women will be able to control their reproductive choices.

Adhering to a medical protocol can be challenged by many factors and can result in patients not getting their injections.

Needles and syringes limit accessibility to necessary medicines and vaccines by requiring a trained medical professional to administer them in clinical settings, and in many parts of the world, trained professionals are not always available.

Self-injection (when approved at the option of regulatory authorities) can address some of those issues. For example, many women cannot routinely get to clinics that offer injectable contraception, while others start using the method but stop because they cannot return to the clinic.[27]

Additionally, many societies discourage contraception for social and religious reasons. Taking pills at home is highly "visible" so many women don't do it.

The ability to self-inject contraceptives can encourage continuation of contraception as it addresses some of the reasons why women discontinue use, such as travel expenses and long distances to the clinic, and long waits at the clinic.[28]

For young women and adolescents, who often have higher rates of contraceptive discontinuation, and who also place a high value on their privacy, self-injection can offer independent and discreet contraception use over a longer period of time.[29]

Self-injectable contraceptives are highly effective, safe, and private, and they increase access and empower women to manage their reproductive health.[30]

With discreet quarterly self-injection, more women will be able to control their reproductive choices. This is confirmed by the World Health Organization (WHO) supporting self-injection where women have access to training and support.[31]

Self-injectable contraceptives that can be offered in low-cost, single-use, prefilled syringes increase choice of affordable contraceptives and have the potential to increase access for women at the last mile and empower them to manage their reproductive health.[32]

Uniject™ an innovative injection technology originally developed in the 1980s, provides a success story for injectable contraceptives and women's health.

Injectable contraceptives address many of the barriers to access faced by women.

One contraceptive option that is particularly convenient for women is injectable contraceptives. They offer many benefits, including safety, effectiveness, different durations of protection, avoidance of using a daily method, and discretion – a woman can use them without the knowledge of her family members.[20] "Injectable contraceptives are an important innovation, which can reach new and younger users who often face high barriers to accessing comprehensive choices," said Bermejo.[21]

Injectable contraceptives are increasingly popular with women around the globe – currently the third most prevalent form of reversible contraception worldwide and rising[22] – as they provide a safe, effective, and discreet method of preventing pregnancy.

The first injectable contraceptive was Depo medroxy-progesterone acetate or DMPA. It was developed in 1954 as a treatment for endometriosis, but it wasn't until the early 1960s when DPMA was considered as a method of birth control.[23]

Today, injectable contraceptives are typically given subcutaneously using the Sayana Press, a "squeeze-bubble" type syringe manufactured by Pfizer, using Uniject™ technology licensed from Becton Dickinson, which provides the syringes as a component. One injection of Pfizer's Depo-Provera with the Sayana Press device inhibits ovulation for at least 14 weeks.[24] (The name "Sayana Press" translates roughly to "smart squeeze.") Injectable contraception is more than 99% effective in preventing pregnancy with consistent use,

and approximately 97% effective as commonly used. It is estimated that 13 million women are currently using DMPA, and the method is marketed in more than 90 countries worldwide.[25]

The innovative Sayana Press syringe uses an injection system originally developed by PATH under the name Uniject™ beginning in the late 1980s. A decade later, PATH partnered with medical device maker Becton Dickinson to manufacture at scale. In 2014, some 250,000 Sayana Presses were distributed in the West African nation of Burkina Faso, which was trying to raise contraception availability from 15% to 25% of women by the end of next year.

PATH and other NGOs are working with local health ministries to finance and distribute the contraceptive devices in Niger, Senegal, Uganda, and Bangladesh soon.[26]

The ApiJect Prefilled Injector* could potentially help with many of the economic, logistical, and cultural problems contraceptives can present.

The ApiJect Prefilled Injector* is intended to offer Uniject's™ breakthrough advantages, but with the ability to quickly scale.

The ApiJect Prefilled Injector is designed for potential ease of use by most teens and adults with minimal training. 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).[33] Prefilled syringes solve this problem but cost is prohibitive for many LMICs. The ApiJect Prefilled Injector is designed to be economically efficient.

If patients had the ability (and regulatory permission) to inject themselves with medicine or vaccine...or if healthcare workers could inject patients in non-clinical settings, because traditional syringes and vials were no longer necessary...many more people in need could be covered. In a world where there is a shortage of healthcare workers, this could be life-changing for millions of people, including an estimated 214 million women in developing countries who have an unmet need for modern contraception.[34]

By making it simple and easy for women to self-inject contraceptives, fewer healthcare professionals or community health workers would potentially be needed. Use of a prefilled format would reduce dependency on health workers to prepare injections by filling syringes from vials.[35] Supporting greater patient autonomy could potentially increase the number of patients who would remain current on their treatment. It could also potentially change the way that many people around the world access and receive contraceptives, in low-resource, non-clinic settings.[36]

*Products shown for informational purposes only, not for use in product promotion.
ApiJect's Prefilled Injector and other products have not been reviewed or cleared by FDA or other regulatory authorities for distribution.

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The opportunity for self-injectable contraceptives to make a contribution to global health is overwhelming. ApiJect can make a difference in women's lives by providing a more efficient, cost-effective way of delivering access to family planning, improving the health and development of communities.

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

Animal health and human health are closely linked. At home, healthy pets make happier, longer-lived companions. On farms, sick animals put human health at risk, while healthier livestock reduces the spread of disease and produces safer food.

"…pet owners [have] started seeing their animals as family, and are desperate to help these family members live longer, healthier, more comfortable lives…

People lavish their pets with love and concern like they do other family members, with total U.S. pet industry expenditures project to rise almost $6 billion in two years to more than $72 billion in 2018."

MICHAEL HELMSTETTER
PRESIDENT, TECHACCEL

"The Future of Animal Health"
Forbes, Aug. 21, 2018[1]

According to the Animal Health Institute, "24 billion chickens, more than 1 billion cattle and sheep, 750 million pigs and goats, 500 million dogs and 400 million cats" worldwide benefit from innovations in animal health.

KATHLYN STONE
PRESIDENT, TECHACCEL

"ANIMAL PHARMACEUTICAL COMPANIES"
The Balance, April 22, 2019[2]

The $45 billion global animal health market is forecast to reach $70 billion in 5 years.[3]

Global animal health includes care for pets and animal companions.

It also includes care for livestock on large industrial farms in High-Income Countries (HIC), as well as animals on tens of millions of subsistence farms and small family farms in Low- and Middle-Income Countries (LMICs).

The global animal health market is enormous and growing fast. In 2017, U.S. pet owners spent an estimated $69 billion on acquiring, feeding and caring for their pets.[4] This includes approximately $15 billion for supplies and over-the-counter medications.[5] According to the American Animal Hospital Association (AAHA), Americans spent $35 billion on veterinary care in 2015.[6]

There were 157 million U.S. pets in 2012, according to industry figures, a number that has grown considerably since then.[7] The world's farm animal population includes roughly 25 billion cattle, chicken, sheep, pigs and goats.[8]

According to the Animal Health Institute, animal pharmaceuticals are used chiefly to treat or prevent diseases or infections. As is true for humans, it is also the case that pets and farm animals receive vaccines to address some diseases and conditions, while receiving non-vaccine medicines to treat other conditions. For example, veterinarians treat animals with pharmaceuticals such as anti-parasitic drugs, anti-inflammatory medications, anesthetics, pain medications, antibiotics, and specialized products for managing reproductive, cardiovascular, or metabolic conditions.[9]

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 and economic impacts, but for the family's physical survival.

Many factors are combining to create growing needs for more and better animal medical care.

Pet owners are buying more pets and lavishing more resources and attention on their animals, including medical care.

Meanwhile the number of zoonotic (animal-to-human) diseases and food-borne diseases is rising significantly.

The global animal health market is expected to see a combined annual growth rate of 5.7% from 2019 to 2026.[10] A number of factors are contributing to this rapid growth.

To begin with, the growing human population drives growth in the animal population. As more families achieve middle class status around the world, they add more pets to the family.

In the farm sector, a growing human population means more mouths to feed around the world. As a result, demand for meat and poultry rises and more livestock is needed to meet this growing demand.

Another critical factor driving the growing demand for animal healthcare is the expanding rate of zoonotic and food-borne diseases around the world, in both HICs and LMICs. In response, pharma companies are working to develop advanced vaccines and medicines that can more effectively prevent and treat the major diseases.

Veterinarians, pet owners and farm owners, in turn, are signaling higher demand for these meds and vaccines in order to keep animals safe and healthy. In the U.S., the government is promoting greater use of veterinary products for the same reasons.

The following pages provide a high-level overview of the pet and farm animal medical sectors in turn.

As the world's pet population grows, the future of pet care is not more visits to the vet; it's more home care.

Around the world, people love their pets and animal companions…and it's no wonder, considering how much pets add to human health and quality of life.

As the U.S. National Institutes of Health has stated, "Nothing compares to the joy of coming home to a loyal companion. The unconditional love of a pet can do more than keep you company. Pets may also decrease stress, improve heart health, and even help children with their emotional and social skills."[11]

The global pet population is large and rapidly getting larger. For example, around the world, an estimated 400 million dogs serve as animal companions to humans.[12] In the U.S. alone, the pet population includes more than 120 million dogs, 130 million cats and 50 million other animals ranging from fish to reptiles, birds and horses.[13]

The American Medical Veterinary Association reports the typical dog is taken to the vet's office 2.6 times per year.[14] Average visit cost: $257.[15] Even 65% of veterinarians believe pet care costs too much.[16]

The world pet population expands as the population and incomes grow. Another factor driving demand for more pet healthcare: owners increasingly treat pets as family members, seeking the best available treatment, comfort remedies and preventatives.

As *Forbes* recently reported, "…pet owners [have] started seeing their animals as family, and are desperate to help these family members live longer, healthier, more comfortable lives…People lavish their pets with love and concern like they do other family members, with total U.S. pet industry expenditures project to rise almost $6 billion in two years to more than $72 billion in 2018."[17]

Many owners do not vaccinate pets, in part due to high costs… but not vaccinating costs more.

Medical injections are a significant portion of pet health expenses, although statistics are both rare and widely varied.

Some sources estimate 500,000 annual injections worldwide drive sales of more than $8 billion/year in pet medicine and supplies.[18] Other sources project China alone sees 100+ million annual injections for pets.[19]

Vaccines are key injectables for animals, with a global compounded annual growth rate of 7.4% thru 2022.[20] Again, costs can seem high. For example, a parvo vaccination by an independent veterinarian in a moderately priced Midwestern market typically costs $35 to $50, plus office visit fees.[21] A package of 3-4 vaccinations plus testing for common diseases costs $99 at a leading veterinary chain store.[22]

Although animal vaccines are a rapidly growing industry, most of the vaccines administered to animals goes to farm livestock (particularly on large industrial farms).

The situation for pets is markedly different, and offers cause for concern. A 2016 survey suggests 53% of U.S. dog owners and 36% of cat owners don't vaccinate their pets at all, or somehow obtain vaccinations outside the veterinarian's office.[23] Cost is one reason, yet skipping vaccinations and waiting to treat an infection often costs far more. Canine parvovirus treatment costs begin at $600 and can amount to several thousand dollars.[24]

Of greater concern, when animal population vaccination rates dip below 70%, herd immunity can be lost, making widespread disease more likely.[25]

On small family farms around the world, human health and animal health are closely linked.

On subsistence farms and small independent farms in Low- and Middle-Income Countries (LMICs), animals are indispensable to human well-being.

The size of the global farm animal population is reflected in statistics provided by International Livestock Research Institute, in Kenya, the UN's Food and Agriculture Organization, and other groups.

These groups estimate that farms worldwide maintain 1.4 billion cattle, 1.9 billion sheep and goats, 980 million pigs, and 19.6 billion chickens.[26]

These animals are not just found on large-scale industrial farms. Hundreds of millions of small family farms worldwide also keep livestock, from dairy cows and goats to sheep and poultry. For billions of people in many LMICs, these animals generate primary income including valuable products such as wool, hair, silk, hides, skins, furs, wax, feathers, bones, horns and more.

In addition, these "living renewable resources" also provide the chief means of physical survival for many families on small farms, serving as their primary source of food since animals and bees 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 word – particularly in LMICs – most of farm animals go unvaccinated and under-treated when they contract disease.

Injectable medicines and vaccines are an important tool for keeping animals healthy, which keeps people healthy.

The fallout from an avian flu infection of U.S. farm animals demonstrates the high cost of allowing animals to get sick.

The 2014 avian flu infected untold numbers of chickens on hundreds of U.S. farms in 21 states, triggering the destruction of more than 50 million infected or potentially infected birds.

Other countries imposed trade bans against U.S. poultry, resulting in a total cost to the U.S. economy exceeding $3 billion.[27]

Clearly, the cost of allowing pathogens to infect animal populations is high in any nation, regardless of national income. The world's farms are expected to spend US$6.5 billion on animal vaccines by 2025.[28] But these vaccines are almost exclusively used in industrial farming operations.

Unfortunately, vaccination rates for farm animals are very low in many LMICs. For example, the UN estimates that only 38% of livestock in Tanzania and 21% in Uganda receive vaccines, and even fewer animals in such countries may receive treatment for parasites and other infections.[29]

Animal infections can have a snowballing effect. As noted earlier, when animal population vaccination rates dip below 70%, herd immunity can be lost, making widespread disease more likely.[30] The applies to livestock as well as pets. Small farms need a new, low-cost, easy-to-implement solution.

Pets and small farm animals get medicine and vaccine injections from traditional syringes and glass vials.

Syringes and glass vials are 165-year-old technology that present many significant drawbacks for global animal health.

From cost to coverage, convenience, adherence, safety and more, syringes and glass vials come with many issues that work against optimal health for animals.

Cost and coverage: Using a traditional syringe that is filled from a glass vial, the TCOD (Total Cost of Delivery) per dose can be quite expensive. Costs vary, but many pet owners and subsistence farmers do not vaccinate their animals due to high costs, leading to livestock deaths and increasing risks of zoonotic disease. Transporting glass vials is also expensive due to weight.

Convenience and adherence: Trips to veterinarians can be expensive and time-consuming, reducing adherence. With regulatory approval, an easy-to-use delivery alternative such as a low-cost prefilled syringe could be deployed by pet owners and small farm owners to inject their animals at home.

Safety: Improperly reused traditional syringes in medical settings lead to contamination of both syringes and multi-dose glass vials, spreading disease. Pets and farm animals worldwide are vulnerable to the same danger that infects 20 million humans annually.

Additional safety issues include delamination (glass flakes shear off inside the vial and mix with the contents) and breakage, forcing costly recalls.

Environmental impact: Billions of glass vials are manufactured each year in a slow, costly, highly energy-intensive process. Their manufacture creates substantial industrial waste, and disposing of empty vials creates still more waste.

Animal injections could potentially be affordable and easier to perform with a prefilled format.

Drug delivery devices for humans have long included squeeze-activated plastic prefilled devices; similar technology could potentially be available for pets and farm animals.

ApiJect plans eventually to develop several different sized prefilled BFS injectors* for animals. Subject to regulatory approval, they could potentially serve the pet and farm animal markets, helping increase coverage.

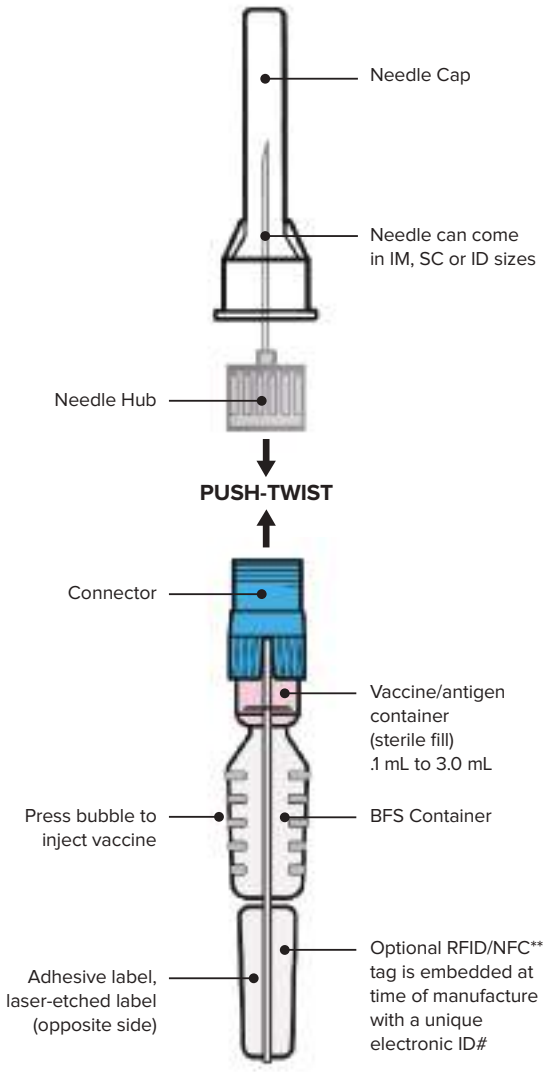
ApiJect envisions formatting each animal injector as a one-dose, single-use, prefilled plastic device. Advanced BFS manufacturing and materials would potentially support economic efficiency and affordability. Since prefilled formats require no filling from a glass vial, and would be precisely prefilled at the time of manufacture, some animal owners could potentially inject their animals without requiring veterinary services.

Because these injectors would be precisely prefilled at the time of manufacture, there is no need for a glass vial and no need for the caregiver to fill the device. Pet owners and farmers could potentially get appropriately sized injectors in bulk by prescription from a vet, then inject their animals at home as instructed. This could avoid long trips from farm to city, and reduce costs through fewer vet office visits. Users would simply squeeze the plastic container to inject the medicine or vaccine.

ApiJect's planned products for animals would feature a special needle hub that supports various needle sizes: heavy-gauge needles for thick hides (cattle, goats, etc.) and lighter-gauge needles for dogs and cats, as well as young calves, pigs and poultry. This specialty hub would not accept needles sized for humans.

A Prefilled Injector for Animals

The BFS container is SEPARATE from the needle, making it easy to mix and match needle sizes for different types of animals.



*Products shown for informational purposes only, not for use in product promotion. **RFID is Radio Frequency ID. NFC is Near Field Communications. ApiJect's Prefilled Injector and other products have not been reviewed or cleared by FDA or other regulatory authorities for distribution.

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