



RAPID USA (Rapid Aseptic Packaging of Injectable Drugs): providing rapid population-scale packaging of vaccines and therapeutics in prefilled syringes with real-time reporting of all injections.

For the first time, the U.S. will be able to produce 330 million aseptically prefilled syringes per month in the event of a pandemic or biothreat emergency.

The U.S. government agency responsible for planning, strategy and implementation of population-scale defenses against pandemic flu and other wide-scale health threats is the Department of Health and Human Services (HHS) — specifically the HHS Office of the Assistant Secretary for Preparedness and Response (ASPR). According to ASPR's Public Health Emergency website, ASPR “oversees advanced research, development, and procurement of medical countermeasures for 21st century health security threats” through its Biomedical Advanced Research and Development Authority.

One of the most significant potential threats for which ASPR seeks to ensure U.S. preparedness is a pandemic caused by a novel virus, such as SARS-CoV-2, the “coronavirus” that spreads the disease known as COVID-19. Other pandemics are possible from diseases such as Ebola, HIV-AIDS, and influenza, also known as the flu. Four times in the last 100 years – 1918, 1957, 1968 and 2009 – a highly transmissible new pathogen emerged that triggered pandemic flu. Resulting fatalities ranged from an estimated 203,000 people worldwide (2009) to perhaps as many as 50 million or 100 million (1918).¹

There is a significant difference between a pandemic such as COVID-19 or even a pandemic flu and the routine seasonal flu, with which most of the public is familiar. Seasonal flu arrives on a predictable timetable every year. It typically kills 250,000 to 650,000 people per year worldwide and infects 1+ billion.³ Fortunately, the pathogens that trigger seasonal flu are strains that most people have already been exposed to and developed some resistance. In addition, because seasonal flu is spread by known pathogens, effective vaccines are already stockpiled or can be prepared relatively quickly.

None of this is true of a pandemic like COVID-19 or

pandemic flu. Its timing is not predictable; and it springs from previously unknown pathogens. That is why the pandemic can spread so far, so fast. In addition, because the pathogen is novel, no existing vaccines can be stockpiled in advance to mitigate against its spread. Fatalities can be significantly higher than for seasonal flu.⁴ According to the White House Council of Economic Advisors, such a pandemic could also cost the U.S. economy \$3.8 trillion in direct immediate costs plus long-term lost productivity.⁵

To defend against this and similar threats, both HHS and the national defense community have devoted substantial resources. Scientists have made significant advances in their abilities to detect outbreaks early, then quickly isolate the pandemic's pathogen, sequence its DNA, and develop a new, well-matched vaccine.

However, pandemics move quickly in this age of jet travel and urbanization. As the COVID-19 outbreak has shown, simultaneous clusters of cases can pop up in a dozen cities across any one country or in many countries around the world. Pandemic response must therefore move rapidly too. In effect, when a pandemic occurs, the U.S. must run a “relay race” against time to vaccinate as much of the population as possible, or give therapeutics to patients who are already infected.

This race includes a sequence of 12 related steps, from recognizing the outbreak at the start of the race, to vaccinating the population at the end of the race. Failing to achieve even one of the 10 intermediate “baton hand-offs” could mean the pathogen spreads virtually uncontrolled through the population. Most of the focus is on producing an effective vaccine or therapeutics in a short period of time. However, several critical steps in this relay race occur after millions of doses have been manufactured. Depending on the scenario, just for U.S. needs, pharmaceutical companies



must acquire, fill and finish 130+ million multi-dose glass vials to contain individual or multiple doses of vaccine and adjuvant (an immunity booster) – enough so that each citizen can receive two injections, 21 days apart.⁷

To administer the vaccine or therapeutics, the U.S. must also acquire some 660+ million syringes. Some of those syringes will be needed to mix vaccine and adjuvant at the point of care, just prior to injection. The rest will be needed to inject the adjuvanted vaccine into subjects.

A major challenge is that the U.S. lacks “surge capacity” to produce great quantities of vials and syringes – and they are not stockpiled in great numbers.⁸ Lead times on large quantities of medical glass vials are at least 6-12 months.⁹ Adequate capacity to “fill and finish” those glass vials is also lacking.¹⁰ Vials require rubber stoppers, crimps and labels, and assembly lines to pour the vaccine into the individual vials and then seal them. Current fill-finish capacity for biologic pharmaceutical demand is minimal and also falls well short of rapid, population-scale surge capacity.

Like glass vials, syringes are not stockpiled in quantities that could cover the U.S. population more than once; and millions of additional units cannot be acquired or manufactured on short notice. Finally, most medical suppliers are located overseas and may not prioritize U.S. needs.

But now, there is a new innovation that will harness the high-volume output of Blow-Fill-Seal (BFS) plastics manufacturing to rapidly produce prefilled syringes in very large quantities. By building a network of relatively small BFS facilities on U.S. soil, the country will acquire the surge capacity to fill and finish bulk antigen for the whole population in a matter of weeks in a pandemic emergency.

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

It is now possible to use BFS to make prefilled syringes the same way, at the same very high speeds, by affixing a Pen-Needle Hub to a BFS Container as part of the manufacturing process. A network of some 30 BFS machines will be able to produce 330+ million BFS prefilled syringes per month, sufficient to cover the entire U.S. population every month.

In addition, the BFS Container will eventually incorporate dual chambers to hold the vaccine and adjuvant separately. These two ingredients would be mixed in an integrated third chamber during the injection process. This simplified injection process for adjuvanted vaccine will eliminate dosing errors and increase the speed of injection. It also eliminates much of the need for surge capacity in glass vials.

Remote, real-time tracking of injections in the field can be achieved by affixing an NFC (Near Field Communication) tag to each BFS prefilled syringe. The NFC tag will hold a unique encrypted serial number. Just prior to injection, the health worker would tap the NFC tag to the back of their smartphone (just like using Apple Pay at a checkout counter).

A free mobile app would capture and automatically upload the dose's serial number, as well as append patient-anonymous data including time, date, and GPS location to the government's designated cloud database. Data would then be aggregated and analyzed to provide real-time coverage maps for more efficient vaccination campaigns.

With participation by the U.S. Government, a new BFS production network for prefilled syringes will be built and operated on U.S. soil. Known as RAPID USA (Rapid Aseptic Packaging of Injectable Drugs), this partnership of government agencies and private industry will raise \$500 million to \$1 billion in private capital to fund construction of 100,000 sq. ft. BFS manufacturing facilities over the next few years.

Meanwhile, with the spread of COVID-19, the U.S. may need population-scale injection capacity on an emergency basis — starting this year — to cover all citizens with therapeutics as soon as they become available.

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

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

May 8, 2020



Pandemic Defense for the U.S. Population

**RAPID USA (Rapid Aseptic Packaging of Injectable
Drugs) will Enable HHS to Deliver Fast, Mass-Scale
Vaccination and Therapeutics in the United States.**

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

— Dr. Walt Orenstein,
Director of the CDC’s
U.S. National Immunization Project, 1993-2004¹

**“Without vaccine supply chains,
vaccines cannot make it to the people.
Without making it to the people,
vaccines can’t do anything. And
when vaccines can’t do anything,
the life-saving and improving power
of vaccines and money invested in
them go to waste.”**

— Forbes Magazine²

SECTION 1:

The U.S. Has Struggled with Pandemic Supply Chain Problems for Decades



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

**Critical links in this chain include:
rapidly acquiring enough glass vials and syringes,
and getting them promptly filled and finished
so mass-scale injections can be administered.**

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

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



PREPAREDNESS FOR PANDEMICS

Despite vaccines, seasonal flu annually infects 1 billion and kills up to 650,000 people worldwide.³

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

Influenza (flu) is a contagious respiratory illness caused by viruses that infect the nose, throat, and sometimes the lungs. The illness can be mild – a few days of coughing, aches and fever – or it can lead to hospitalization and even death. Up to 11% of the U.S. public contracts influenza in any given year, according to the U.S. Centers for Disease Control and Prevention (CDC).⁴ Many strains of seasonal influenza virus exist, and they are

constantly evolving, sometimes mutating through multiple generations in a single year. Influenza viruses circulate in different times in different places around the world. In temperate regions, such as the U.S. and the rest of the northern hemisphere, influenza epidemics occur in late fall and winter. In contrast, influenza circulates most frequently in the southern hemisphere from May to September, so the world as a whole has two “flu seasons” in each calendar year.⁶

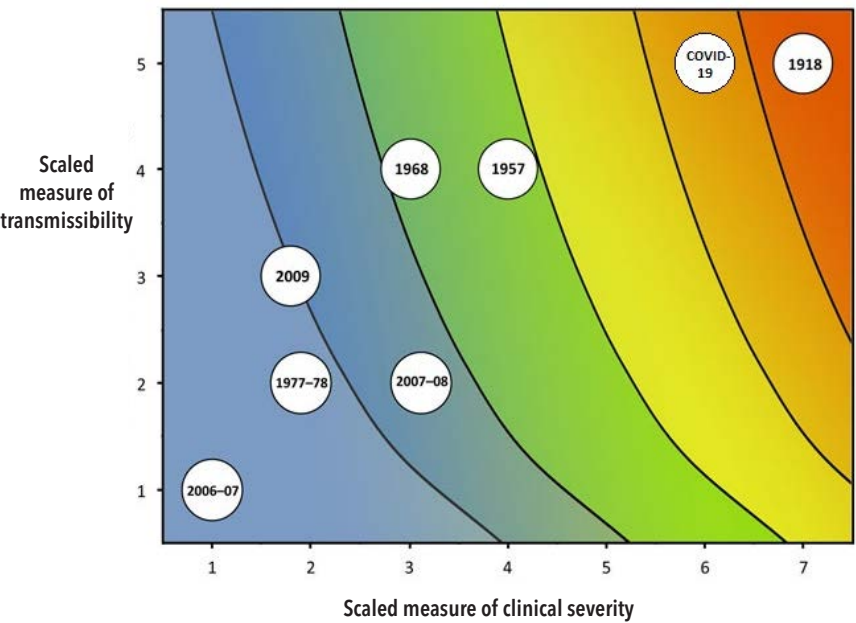
Even though the typical virus that drives seasonal flu is constantly changing, it is usually one that is closely related to a strain that has recently circulated. But at unpredictable intervals, a new strain of influenza emerges, creating a novel and unpredictable strain that humans have never faced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

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

“An influenza pandemic occurs when a new influenza virus emerges and spreads around the world, causing large numbers of illness and deaths, as most people will not have immunity to the new virus. Influenza pandemics can be mild, moderate or severe.”⁷

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

Pandemic Severity Assessment Framework (PSAF): Pandemic Influenza and Epidemic Influenza Severity⁵



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

PREPAREDNESS FOR PANDEMICS

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



“Seasonal and pandemic flu preparedness are closely linked, given that vaccine production for seasonal flu viruses is the foundation for vaccines production for a pandemic flu,” according to a September 2019 report by the U.S. Council of Economic Advisers (CEA).⁸

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



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

“The main method of producing [seasonal] flu vaccines currently in use relies on production in chicken eggs and takes six months or more to produce adequate doses of vaccine [for population-wide coverage],” explained the CEA, which cited WHO when it added: “Essentially, the same 6-month, egg-based process is used to make vaccines in the case of pandemics.”⁹

Accordingly, any vaccine intended to combat a large-scale pandemic during the first wave of disease spread “would arrive too late to avert a meaningful number of infections and deaths,” according to that same CEA report.¹⁰

PREPAREDNESS FOR PANDEMICS

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



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

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

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

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

weeks or even days. The flu virus spreads quickly.

According to WHO, "It takes approximately five to six months for the first supplies of approved vaccine to become available once a new strain of influenza virus with pandemic potential is identified and isolated."¹¹

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

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

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

PREPAREDNESS FOR PANDEMICS

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



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

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

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

At first glance, this change of formats may appear to

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

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

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

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

PREPAREDNESS FOR PANDEMICS

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



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

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

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

Even without a pandemic or other bio-emergency and a surge of demand for emergency services, this stage of the medical supply chain already creates a significant bottleneck for pharmaceutical companies attempting to get their current products to market.¹⁴ Like glass

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

Questions over the sufficiency of available fill-finish capacity have long been a concern for the HHS Assistant Secretary for Preparedness and Response.¹⁵ Although the U.S. has currently arranged for a few domestic companies to fill and finish enough 10-dose glass vials for each citizen to receive a single injection, multiple injections may be required for robust pandemic defense — in which case, U.S. capacity for speedy fill-finish operations may be stretched to the limit or beyond. This vulnerability has been identified by the World Health Organization as a significant potential bottleneck in population-scale vaccine delivery.¹⁷

PREPAREDNESS FOR PANDEMICS

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



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

According to Dr. Robert Kadlec, the HHS Assistant Secretary For Preparedness and Response, “The U.S. lacks sufficient domestic manufacturing capacity and/or raw materials for almost all pandemic influenza medical countermeasures, including vaccines and therapeutics, [and] the needles and syringes needed to administer them...”¹³ This shortfall applies to all pandemics.

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

shut down by wind, water and power failures, shipments of saline bags to U.S. hospitals came to a halt. As a result, these hospitals quickly ran through their limited local inventories of saline bags. Medical staff began using syringes to inject saline into patients. But then, hospitals began running out of syringes.¹⁸

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

In the face of a potential mass outbreak, federal officials might have to invoke the Defense Production Act to press America’s private industry into service on behalf of the nation’s health.¹⁹ But most syringe manufacturers are located abroad and not subject to the requirements of the law.

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

“Further, in a pandemic, global manufacturing capacity will likely not be sufficient to meet demand, resulting in an inability to import adequate quantities of medical countermeasures.”²⁰

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

SECTION 2:

We Will Strengthen the U.S. Pandemic Supply Chain



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

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

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

As a public-private partnership, RAPID USA will build and operate 30+ cold-chain production lines inside several U.S.-based facilities.

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

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

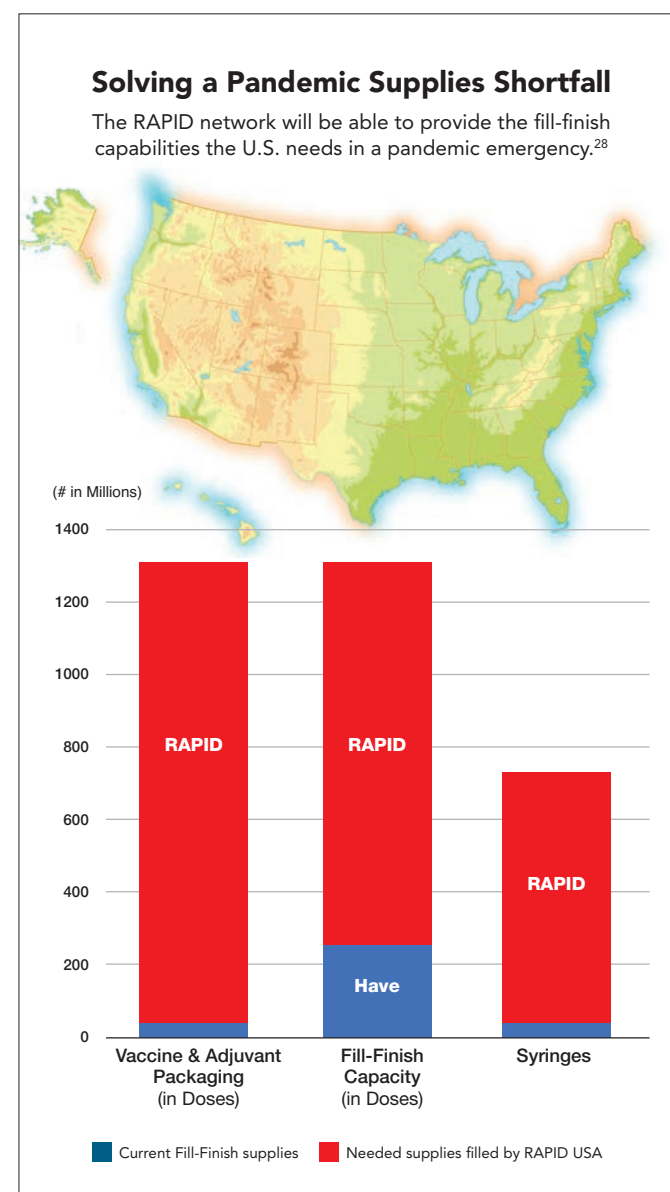
The ability to create prefilled syringes from Blow-Fill-Seal (BFS) plastic manufacturing technology will allow the U.S. government to defend its population quickly and efficiently when a severe pandemic or other biological threat emerges.

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

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

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

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



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



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

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

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

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

PREPAREDNESS FOR PANDEMICS

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

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

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

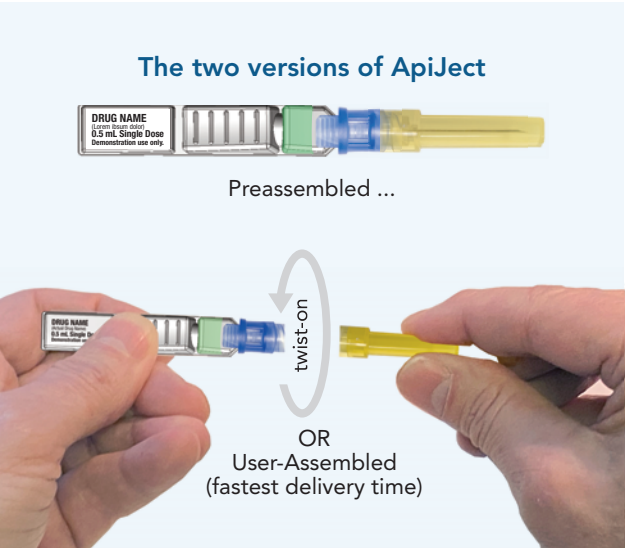
The result is a new type of prefilled, single-dose, one-use syringe that can be produced in extremely high numbers, and with extreme speed. A single BFS machine, roughly the size of a truck, can produce up to 20 million FDA-approvable finished doses per month, packaged in prefilled syringes and ready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

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

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



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



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

PREPAREDNESS FOR PANDEMICS

Blow-Fill-Seal (BFS) is an FDA-approved technology to manufacture, fill and finish sterile drug containers.²¹



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

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

Around the world, BFS technology is currently used to manufacture 50 billion low-cost plastic “squeeze-bottle” containers every year. Contents include sterile eyedrops, eardrops and nasal sprays as well as a limited number of oral vaccines.²² BFS technology can safely package most liquid biologicals, including vaccines that are suitable for medical countermeasures.

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

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

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

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

The agency’s 2004 publication, “Guidance for Industry – Sterile Drug Products Produced by Aseptic Processing,” remains its current statement on BFS standards. That document notes: “Advantages of BFS processing...include rapid reservoir closure processing and minimized aseptic interventions.”²³

PREPAREDNESS FOR PANDEMICS

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



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

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

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



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

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

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

PREPAREDNESS FOR PANDEMICS

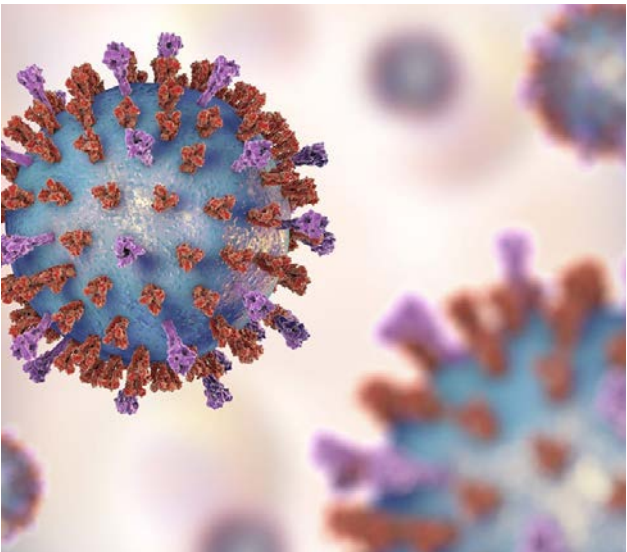
Pandemic vaccine may need to be mixed with an “adjuvant” (immunity booster) at the time of injection.

As defined by the CDC, an adjuvant is “an ingredient (such as certain aluminum salts) used in some vaccines that helps create a stronger immune response in people receiving the vaccine.”²⁴

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

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

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

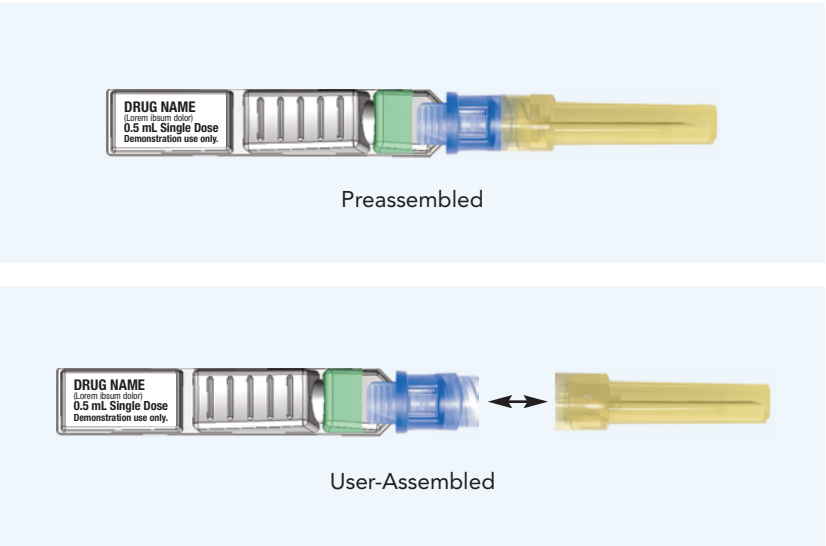


vaccine that protects against seasonal influenza), the BFS facilities will prefill syringes with the precise mixture. If adjuvant and vaccine must be mixed at the point of care, a dual-chamber variation on the basic BFS design will contain vaccine in the first sealed chamber, and adjuvant in a separate,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



PREPAREDNESS FOR PANDEMICS

Advantages of BFS-enabled prefilled syringes include safety, anti-counterfeiting and faster injections.



BFS manufacturing has previously not been used for syringes. A widely used component called a Needle Hub, adapted to BFS, makes it possible.

Previous “squeeze bubble” plastic syringes used slower, more expensive multi-step manufacturing, a weeks-long resin layering and curing process that forecloses the possibility of rapid, population-scale supply.

Integrating a sterile BFS “squeeze-bubble” container with a connector, Needle Hub and double-ended hypodermic needle makes it simple, fast and convenient to use any of the standard-sized needles.

The result is a “soft syringe” with no barrel and plunger, and no need for a glass vial. An example is the ApiJect prefilled syringe from ApiJect Systems Corp. With a prefilled syringe, there is no need for glass vials, greatly

reducing response time for vaccine campaigns. Once used, the syringe’s container collapses and cannot be refilled or reused.

Preventing reuse is important to block the spread of blood-borne diseases from used syringes. In addition, the needle cannot be separated from the device and reused.

In a pandemic, counterfeiting is a special danger. A BFS prefilled syringe can include features enabling users to quickly verify that the syringe and its contents are new and genuine.

Numerous studies have shown that prefilled syringes reduce injection time compared to multi-dose vials.²⁵ A prefilled dual-chamber syringe will further reduce injection time for adjuvanted vaccines that must be mixed at the point of care just before injection.

PREPAREDNESS FOR PANDEMICS

BFS prefilled syringes enable real-time remote tracking of injections nationwide with low-cost mobile-ready RFID.

An NFC tag on every BFS prefilled syringe can put every injection on the Internet of Things.

Effective pandemic defense requires officials to accurately monitor in real time how rapidly thousands of clinics are vaccinating local populations, including how many people are being vaccinated and where.

Ideally, health officials would have real-time, continually updated coverage maps and reports, based on data steadily flowing in from across the nation, showing when and where each injection takes place. They would see where broad and effective coverage is happening, and where and when coverage is lagging – patterns that would enable officials to better manage their vaccination campaigns, coordinate supplies, etc.

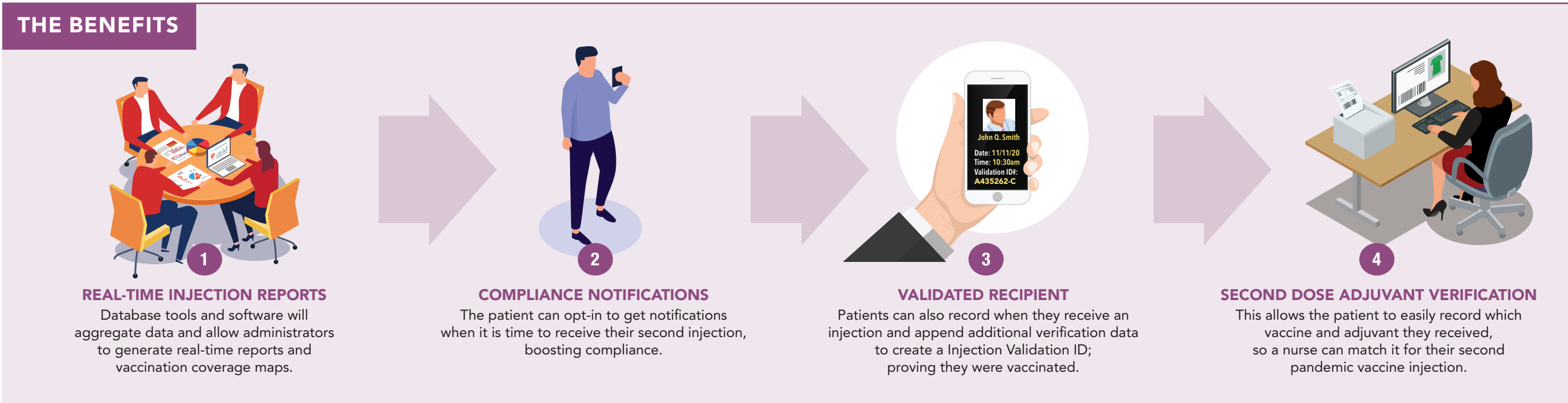
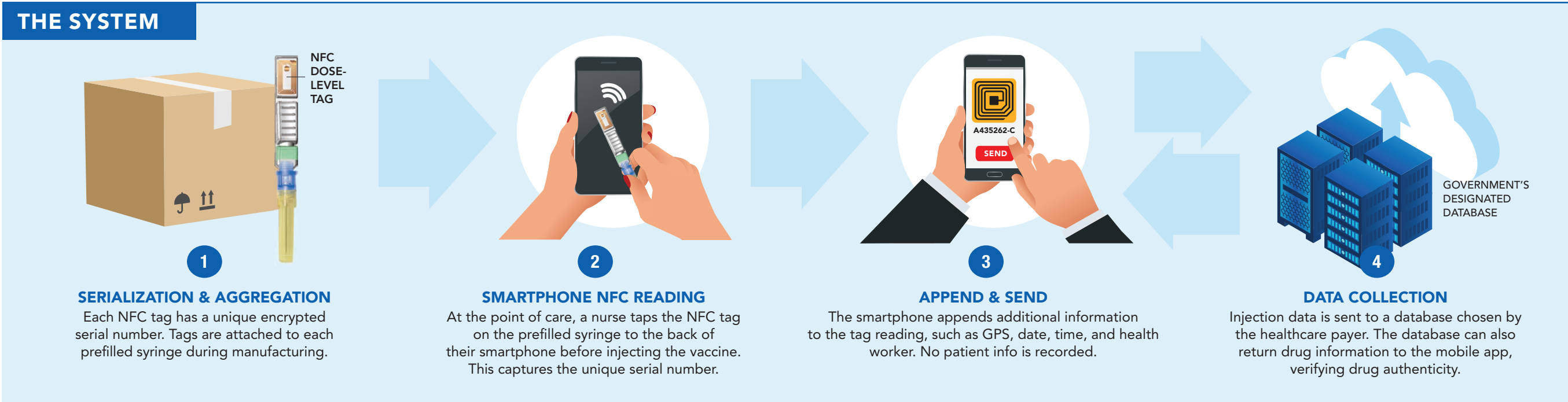
All this can be accomplished efficiently and economically by having RAPID USA manufacture each BFS prefilled syringe with a low-cost Near Field Communication tag on the syringe label. Before each injection, healthcare workers tap their smartphone to the NFC tag, using a free mobile app. Their phone captures a unique serial number from the tag, appends date, time, and GPS location, and uploads these metrics to a cloud database. This anonymous, aggregated data is then used to generate useful reports.

This technology can also support “Injection ID Validation” confirming an individual has been vaccinated (where permitted). Other features can include compliance reminders to people that it is time to get their second dose, and record keeping that makes sure the patient receives the same adjuvant across both injections.



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

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



PREPAREDNESS FOR PANDEMICS

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

RAPID USA, a public-private partnership, will bolster U.S. pandemic defense.

“[Pandemic preparedness] is like a chain—one weak link and the whole thing falls apart,” according to one of the U.S. government’s most experienced health scientists. “You need no weak links.”²⁶

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

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

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



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²⁸ The supplies and fill-finish capacity needed are based on a scenario where the U.S. population needs two vaccinations, at least 21 days apart, with adjuvanted pandemic flu vaccine to provide adequate protection against the novel virus. This scenario envisions that adjuvant is packaged separately from pandemic vaccine and is mixed with vaccine prior to administration (one of several possible planning scenarios). Approximately 660 million vaccine doses will be needed, based on the U.S. goal of ensuring that there is enough “pandemic vaccine for everyone in the U.S. who wants to be fully vaccinated against this emerging virus.”*, This will require securing enough glass vials for both vaccine and adjuvant.

Some of this need may be met (if the timing works out), by harnessing seasonal flu vaccine supplies. We assume that 30% of the ~160 million doses of seasonal flu vaccine is filled in 10-dose vials, and 70% are in pre-filled syringes. Since it is not currently known if pandemic vaccine will require an adjuvant and whether it can be packaged with adjuvant, this scenario envisions all pandemic vaccine will be packaged separately in 10-dose glass vials. We also assume that the capacity to fill an additional 100 million vials could be accomplished through existing emergency agreements between HHS and various facilities in the U.S.

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

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The U.S. Department of Health and Human Services Assistant Secretary for Preparedness and Response stated in a 2010 report:

“The Nation currently lacks the domestic manufacturing capacity to rapidly produce and package a vaccine for the American public in the face of a pandemic.”²⁹

RAPID USA will ensure that the United States acquires this critical capacity.



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