2007-2008 Influenza Vaccine Production and Distribution

For the 2007-2008 flu season, early projections suggest that as many as 130 million doses of influenza vaccine may be available for the U.S. market, depending on production yields. Although influenza vaccine manufacturers are currently producing vaccine at or near full capacity, it isn't possible for all of the doses to be produced and distributed before the beginning of the vaccination season.

You may be thinking, “that sounds like a lot of vaccine—why isn’t it ready or at my location now?”

The process of getting influenza vaccine where it needs to go is complex. This vodcast is intended to walk clinicians, public health partners, and other vaccinators through the process, providing a better understanding of vaccine distribution.

Before we discuss distribution, let’s start at the beginning—with production.

Influenza vaccine production begins as early as 9 months before vaccine becomes available. Each production cycle begins by selecting the strains that are the best match to the flu strains anticipated to be circulating during the upcoming flu season.

Completed lots of vaccine become available over a range of several months, from July through the following January. The manufacturing process has many critical and time-sensitive steps; *delay at any point during these steps can result in delays in the availability of influenza vaccine.*

Up through January and February of the prior year, World Health Organization Collaborating Centers, including CDC, identify and analyze circulating influenza virus strains from around the world.

The FDA then distributes candidate vaccine strains to manufacturers for them to prepare high-yielding seed viruses, and to begin vaccine production.

At this point, we’re ready to talk about the actual manufacturing process.

Here to help us with that are Doctors William Atkinson and Larry Pickering.
Hello, I’m Doctor William Atkinson, a medical epidemiologist at the National Center for Immunization and Respiratory Diseases at the Centers for Disease Control and Prevention. With me here today is Doctor Larry Pickering, Executive Secretary of the Advisory Committee on Immunization Practices at the Centers for Disease Control and Prevention.

Welcome, Larry. Thank you, Bill, good to be here.

Mass production of each of the 3 virus strains is the next step, occurring from January to July. Each of the 3 candidate vaccine strains is produced separately by injecting live virus into millions of fertilized hen's eggs.

Each production batch of vaccine is incubated in the eggs for several days to allow the virus to replicate. The virus-containing fluid is then harvested from the eggs. Influenza viruses intended for the injectable vaccine are then inactivated, and virus antigen is purified.

As you can imagine, Bill, there are other challenges that may arise before and during this phase of manufacturing. These challenges include: the number of eggs needed must be estimated 6 months prior to production, which makes it very difficult to adjust for increased demand for vaccine or other factors; or it's also possible that the new strains won't grow well in these hen's eggs; or there could be contamination of vaccine product.

For example, in 2004-2005, United Kingdom regulators suspended production at a manufacturing plant for contamination of its vaccine, resulting in the widely publicized loss of nearly half of the U.S. vaccine supply for that season.

And we're dealing with real eggs here—not the sturdiest of media.

So what happens next? The manufacturing process continues from June through October, when purification and testing are done. For the inactivated, injectable vaccine, virus-containing fluid undergoes multiple purification steps and chemical treatment to inactivate and disrupt the virus.

For LAIV, the live, attenuated influenza vaccine, which is given as a nasal spray, the production process is different.

The manufacturers then begin putting doses into vials, syringes, or nasal sprayers while waiting for FDA approval to release lots; however, each lot must be approved separately for release by the FDA prior to shipment.

In fact, quality control testing by manufacturers and FDA accounts for the majority of production time. Manufacturers and the FDA test vaccine at multiple stages of production to ensure it is safe and appropriate for administration.

The estimated time it takes to grow virus to manufacture one lot, roughly equivalent to 400,000 to 500,000 doses of vaccine, is about 10 weeks-- *without* encountering any production issues. ANY problems encountered during production may cause shortages or delays.

Another major contributor to disruptions in supply and distribution has been that very few manufacturers were providing influenza vaccines to the U.S. market. Difficulties at any one manufacturer had substantial impact on vaccine availability. But, there's good

news. A recent increase in the number of vaccine manufacturers should continue to improve the amount of vaccine available and provide for more stability in the vaccine supply. This permits an increased ability to recover from vaccine production problems that may arise with a single manufacturer.

At this point, we've talked about the manufacturing and production process. But that still doesn't get the vaccine into the vaccinators' hands.

As you probably know, different types of vaccine providers receive their vaccine from different sources. There are several sources. A provider may order influenza vaccine: directly from the manufacturer; from a distributor, who is a customer of the manufacturer; or even from a secondary distributor, from whom the provider also receives other medical products.

Now, it's my understanding that some of these routes of distribution are more direct than others, which could affect the timing of vaccine delivery. Many private providers order from a secondary distributor with whom they have a previous relationship. This may mean that their vaccine goes through many more steps than if they had ordered vaccine directly from a manufacturer. Regardless of which pathway a provider uses to order influenza vaccine, because of the unpredictability during the production process, the time in between shipments may result in the provider running out of vaccine before his or her next shipment arrives.

I think that because some community-based clinics—such as a large pharmacy chain or supermarket—are so visible, other providers may conclude that vaccine has been distributed preferentially to this type of vaccinator. Influenza vaccine production and distribution are primarily private sector endeavors, and decisions about how much vaccine will be produced in a given season are based on several factors, including demand for the product.

Larry, how do current ACIP guidelines play into all this, if at all? Well, current ACIP guidelines recommend vaccinating 75% of the U.S. population, as well as anyone who wishes to reduce their risk of acquiring influenza infection or spreading the disease to others. A diverse group of vaccinators and vaccination settings are needed to accomplish this goal and therefore, the CDC values all health care professionals who provide vaccine.

That's really important because demand is likely rising due to demographic changes in the U.S, creating growth in the size of the target population; expansion of the target population recommended for the vaccine; and increases in the number of healthy people who obtain the vaccine to protect family members and minimize work loss and suffering due to influenza illness.

Bill, many people targeted for influenza vaccinations are not vaccinated by the end of November. It's very important to note that in most years, the influenza season in the United States does not peak until January or February. Therefore, influenza vaccination

should continue throughout the entire influenza season. In most years, vaccination even beyond December is medically beneficial and necessary in order to protect as many people as possible. Let's remember, though, to maximize the benefits of influenza vaccine, it should be given to as many people as possible before the start of influenza activity, considering that it takes two weeks to develop an immune response.

Many patients who are recommended to receive vaccine aren't vaccinated, and the power of a provider recommendation is very important. Remind patients that flu vaccination can continue well into the season—throughout the late fall and winter, including during and after the holiday season.

This year's National Influenza Vaccination Week will be the week after Thanksgiving, November 26th through December 2nd. CDC encourages clinicians, partners, and other vaccinators to plan clinics and education that week and beyond in order to reach those not vaccinated earlier in the fall.

I'm Matthew Reynolds for the CDC.

Thank you for joining us.