Q&A: How to make and distribute a vaccine

October 22 2020

Credit: National Cancer Institute

A number of vaccines to combat the SARS-CoV-2 virus and the disease it causes, COVID-19, are currently undergoing various testing regimens. NC State's Biomanufacturing Training and Education Center (BTEC) helps train the next generation of pharmaceutical workers. The Abstract spoke with BTEC's Dr. Jennifer Pancorbo, director of industry programs and research and an expert on vaccine manufacturing, to find out more about the vaccine production and manufacturing process taking shape in response to the pandemic.

The Abstract: What is a vaccine?

Jennifer Pancorbo: Vaccines are used to combat and control diseases that affect public health. Many vaccines attempt to mimic the disease agent, rather than providing an actual inactivated virus. The initial stage is designing a vaccine that targets the disease. Most vaccines are based in biological processes. So they are made from an organism, like a bacteria or a yeast or a virus, that can yield a particle or protein of interest that will serve as the active ingredient in the vaccine.

TA: How is a vaccine created?

JP: This work takes place in a bioreactor—a fancy bucket with a stirrer and some hoses to inject nutrients—where processes occur to expand the host organism and express the protein or particle of interest. Once the desired compound has been separated from the "soup" in the bioreactor, it needs to be purified. It then needs other components so it can be stabilized and transported. It also needs packaging in a vial or syringe and then those are placed in boxes or cartons that may have different temperature requirements; some may need to be frozen, others may be stored at room temperature. It takes years to make a vaccine as stable as you need, as vaccines need to reach the far corners of the world. Vaccines generally become more fine-tuned as improvements are made over time.

TA: What are the steps needed to show a vaccine is safe and effective?

JP: Vaccines must be proven safe and effective in three stages, or phases.

In Phase 1 vaccine trials, the top concern is safety and ensuring people

aren't adversely affected by problems ranging from pain and rash where the vaccine is administered to death. Around 35-50 people are typically included in Phase 1 trials. If there are side effects, the trial is halted to study whether the problem stems from an individual reaction or from the vaccine itself. Phase 1 could also include fine-tuning the dosage amount.

Successful Phase 1 trials then enter Phase 2 trials, which examine the dose and efficacy of that particular dose alongside a continuation of safety profile. Hundreds of people are tested during this phase, with a good representation of all ethnicities desired. The initial group tested for vaccines includes those of working age—18 to 55 years old. In this phase, vaccine producers compare the statistics between a placebo group that does not receive the actual vaccine and a group that receives the vaccine. Efficacy rates in the 40-50% range appear to be the standard for the SARS-CoV-2 vaccine. There is no vaccine that is 100% efficacious.

After successful Phase 2 trials, the vaccine enters Phase 3 trials, which test thousands of people. There are more safety checks in place and a more fine-tuned process. Employees working in production facilities must be thoroughly trained, for example. Manufacturing thousands of doses is much more complex. Recruiting and screening volunteers for the testing—and the testing itself—takes a good deal of time. Vaccine producers also need to equip their facilities to manufacture the thousands of doses necessary to complete the trial and implement processes to guarantee manufacturing consistency and safety.

TA: How similar is a SARS-CoV-2 vaccine to the yearly influenza vaccine?

JP: Unique diseases require unique vaccines. All vaccines are manufactured under good management practices; which implies that a

regulatory authority is regulating those practices. So the approval process for a SARS-CoV-2 vaccine is similar to the process for an influenza vaccine. But there are so many unique approaches to creating a SARS-CoV-2 vaccine.

From the manufacturing side, then, we can say it's much different than the yearly influenza vaccine.

TA: How long would it take to ramp up mass production of vaccines?

JP: Assembling and purifying the compound of interest is difficult. Scaling up to mass production is very difficult. One of the vaccine production companies uses an RNA vaccine platform to combat SARS-CoV-2. That platform does not currently exist for large manufacturing of any other vaccine. Making RNA is very expensive. Another company uses an adenovirus for its version of a SARS-CoV-2 vaccine and runs an adenovirus platform; adenovirus technology already has a proven process and the bioreactors exist, so the company would need to make some modifications to a system that already exists..

Better manufacturing consistency and efficacy come with having more time to mass produce a vaccine. When you speed up the process you generally compromise your efficacy. It's unlikely that we'll be able to produce enough vaccine to distribute globally by next summer.

TA: Will one corporation have the capacity to manufacture enough of the vaccine to distribute it to the world?

JP: Traditionally, each company has its own technology and commercializes its own product. A number of companies are currently

working on a SARS-CoV-2 vaccine. Those with already existing production and manufacturing lines will have an easier time than those without existing lines.

It also depends on whether all vaccine ingredients are manufactured in one location and whether the manufacturer has multiple production facilities around the world. Having production or manufacturing hubs in different countries or parts of the world is much more efficient than having just one.

Most distribution starts locally. For example: a vaccine produced in North Carolina would likely be distributed first in North Carolina, then the Southeastern U.S, then the rest of the U.S. and then the world.

TA: Is equipment brought in from elsewhere to a central manufacturing site? Or will there be multiple vaccine manufacturing sites around the world?

JP: It's possible that the bioreactor for a SARS-CoV-2 vaccine does not exist. You can't just buy some of this equipment off the shelf.

Much depends what agreements are in place. Companies generally have agreements with governments to produce and distribute pharmaceuticals. The willingness of companies to combine forces to protect people from SARS-CoV-2 appears genuine, but worries exist over sharing knowledge and technology.

The best-case scenario would be for a couple of candidates to produce a successful vaccine, and companies and governments across the globe pitch in to help.

There are a number of global government-owned companies that

produce pharmaceuticals, including ones in Brazil and Thailand. BTEC has trained many of these organizations. These companies could collaborate with private companies to help produce and distribute a vaccine. The World Health Organization and the Gates Foundation are other non-government organizations that have invested in this type of infrastructure.

Provided by North Carolina State University