

Staying Healthy

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SARS-COV2 a/k/a COVID 19 Vaccine Research Development

Early this year, vaccine developers, universities and medical centers began working on vaccines to protect the public from COVID-19. We have heard both concerns and hopefulness about the use and timing of a vaccine. COVID-19 is new and not all of our initial responses have been successful. In this discussion, we will identify critical issues related to development of a vaccine, what the development process entails and what are considered to be the most promising vaccines at this time.

Five pharmaceutical companies, who are developing COVID-19 vaccines that could be used in the United States ["U.S."], include AstraZeneca, Pfizer, Moderna, Johnson & Johnson, and Merck. This week, these pharmaceutical companies provided a subcommittee of the House of Representatives information about vaccine development related to efficacy, price and availability of COVID-19 vaccines. The vaccine developers state they are encouraged by early data that has been generated by their clinical research teams. Three of the five believe they will be able to deliver a safe and effective vaccine near the end of 2020 or early 2021. See <https://www.biospace.com/article/house-subcommittee-grills-vaccine-developers-on-efficacy-price-and-availability/>; See also <https://www.nytimes.com/2020/06/03/us/politics/coronavirus-vaccine-trump-moderna.html>

We will learn more about these three vaccine developers who appear to have the ability to provide vaccines in the U.S. in late 2020 or early 2021. One of these three developers is currently in a Phase III (final) research trial for a vaccine for COVID-19. The other two developers plan to begin a Phase III research trial later this month. Being in a Phase III clinical research means these developers have what may be a "promising" vaccine.

Issues of Concern with COVID-19 Vaccine Development

There are some important issues to keep in mind as we consider the "promise" of a vaccine. These issues are important to the researchers in development of a COVID-19 vaccine.

The first issue relates to the vaccine standard set by the U.S. Federal Drug Administration ["FDA"]. The standard for a vaccine is only 50% efficacy. There is also concern that political pressure may push the FDA to reduce the 50% standard lower. The lower we make the efficacy percentage, the more the efficacy of a vaccine is impacted. <https://www.fda.gov/media/139638/download>

Second, individuals who have been infected with COVID-19 have not continued to show antibodies over time from the infection. For that reason, there is concern these individuals could become infected with COVID-19 again. Similarly, because of the failure to retain immunity from a COVID-19 infection, there is a concern that a vaccine may not create a lasting immunity to COVID-19. The durability of immune response to the vaccine will be followed for one year after the vaccinations for Moderna's research and likely for other vaccine developers. <https://www.ecdc.europa.eu/en/covid-19/latest-evidence/immune-responses>

Third, we have seen COVID-19 attack not only the lungs, but also attack the kidneys, the neurology system and in some children a response similar to Kawasaki's disease (cardiac system), etc. It makes some of us question whether there may be different strains of COVID-19.

Fourth, increasing age has been found to significantly decrease immune response, and to be a significant issue for the ability of seniors to generate neutralizing antibodies. This combined with a possible efficacy of 50% is concerning. Since seniors appear to be at the greatest risk with COVID-19, it is important that the vaccine protect those 65 years of age and older. See <https://www.nytimes.com/2020/06/19/health/vaccine-trials-elderly.html>

Clinical Research Phases for Vaccine Development

It is important to understand the clinical research process in vaccine development.

Clinical development of a vaccine goes through a three-phase process. If the clinical vaccine developers successfully complete Phase III - the final phase - they will likely receive approval by the U.S. Federal Drug Administration ["FDA"] to utilize the vaccine, that has been under research study, for use with the general public. <https://deep6.ai/the-clinical-trial-process-for-a-covid-19-vaccine/>

Vaccine development through clinical research is divided into three phases prior to approval.

- **Phase I:** A small group of people receives the trial vaccine.
- **Phase II:** The clinical study is enlarged and vaccine is given to people who have specific characteristics (such as age and physical health) similar to the population(s).
- **Phase III:** When a vaccine makes it successfully through Phase I and Phase II, the vaccine development goes on to Phase III. At this point, the vaccine is considered "promising." In Phase III, the vaccine is given to thousands of people to determine, among other things, how many people, who were given the vaccine, become infected as compared to the placebo group. During this phase the vaccine

is tested rigorously for efficacy and safety. When a vaccine developer completes the Phase III trial, federal regulators carefully review the information learned from the Phase III trial and determine whether to approve the vaccine and license it for distribution.

- **Phase IV:** Despite, language that vaccine development is a Three Phase process, many vaccines that have been licensed for distribution following Phase III, do undergo a Phase IV to continue monitoring the vaccine to determine if other efficacy and safety issues might could arise in the larger general population.

Promising Vaccines in Development for COVID-19

For purposes of this paper, we will only look at “promising vaccines.” We define “promising” as those vaccines who have successfully completed the first two phases of the FDA for vaccine development. Additionally, we define “promising vaccines” as those vaccines that may be used in the U.S. and are currently conducting a Phase III research study or will begin a Phase III research trial in July of 2020. The vaccine companies who qualify under our definitions are: 1) AstraZeneca, 2) Pfizer and 3) Moderna.

The University of Oxford and Pharmaceutical Giant AstraZeneca [“AstraZenca”].

According to the World Health Organization, AstraZeneca is the leading and first company to have already officially launched a Phase III trial of its vaccine. AstraZeneca officially began its Phase III trial in early July 2020 with thousands of participants. See <https://www.hindustantimes.com/india-news/british-pharma-major-astrazeneca-ahead-in-global-race-for-covid-19-vaccine-all-you-need-to-know/story-wAc0QNcBaul7VyDUzOie8J.html>

According to various media reports in *The New York Times* and *Bloomberg News* along with *The Lancet* (world renowned British medical journal), this promising vaccine for COVID-10 has been developed through the University of Oxford and the British-Swedish Pharmaceutical company AstraZeneca. Again, this is the only vaccine developer that has begun a Phase III trial – the final trial to show whether the vaccine will be approved by the FDA. See <https://www.bloomberg.com/news/features/2020-07-15/oxford-s-covid-19-vaccine-is-the-coronavirus-front-runner>

AstraZeneca’s vaccine is made from a weaker version of a chimpanzee’s common cold virus (adenovirus). Through genes of the spike protein that trigger the production of vaccine against COVID-19 virus that allows the immune system to attack and destroy the virus.

Notably, AstraZeneca testing through Phase I and II showed a “strong antibody” response critical to immunity from the vaccine. On the July 21, 2020 news, it was reported that the United States was purchasing 300,000,000 of the AstraZeneca vaccines., See [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)31604-4/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)31604-4/fulltext)

AstraZeneca has reported its vaccine increased levels of both protective neutralizing antibodies and immune T-cells that target the virus. Clinical Phase III studies are already occurring in the UK and larger clinical studies will also begin shortly in the U.S.

AstraZenca Vaccine: ChAdOx1 nCoV-19

Age of Study Participants in Phase I and II: 18–55 years of age.

Side Effects Shown in Phases I and II: Mild to moderate fever, headaches, muscle aches and injection site reactions that resolved during the course of the research study.

Dose: Injection of an initial dose followed by a second dose 28 days later.

Predicted Use: Provided all goes well in AstraZeneca’s Phase III study, AstraZeneca expects to have approval by fall of 2020.

Availability: AstraZeneca has stated that billions of doses of the vaccine could be manufactured following approval by the FDA.

German Company BioNTech and Pfizer.

Pfizer and the biotech firm BioNTech [“Pfizer”] have developed an experimental COVID-19 vaccine that provided an immune response in healthy patients.

By using messenger RNA to target antigens, the Pfizer vaccine produces antibodies in the human subjects to halt COVID-19. The antibodies were produced at or above levels measured in the blood of people recovering from COVID-19. In addition to producing antibodies, immune T cells that respond to the virus were also produced.

When Pfizer determines a vaccine dose level that is proven to be safe and effective, seniors will also be immunized and followed.

The first clinical data on the vaccine from Phase I and II trials was disclosed in a paper on medRxiv, a preprint server, meaning it has not yet been published in a peer-reviewed journal unlike AstraZeneca and Moderna.

See <https://www.medrxiv.org/content/10.1101/2020.07.17.20140533v1>

Based on the results of Phase I and II trials, the F.D.A. gave the Pfizer vaccine fast track status on July 13, 2020 which speeds up the approval process. Fast Track is designed to facilitate the development, and expedite the review, of new drugs and vaccines that treat or prevent serious conditions that have the potential to address an unmet medical diagnosis.

“We still have a ways to go and we’re testing other candidates as well,” said Philip Dormitzer, the chief scientific officer for viral vaccines at Pfizer’s research laboratories. “However, what we can say at this point is there is a viable candidate based on immunogenicity and early tolerability safety data. <https://www.statnews.com/2020/07/01/covid-19-vaccine-from-pfizer-and-biontech-shows-positive-results/>

“The Trump administration on Wednesday announced a nearly \$2 billion contract with the pharmaceutical giant Pfizer and the smaller German biotechnology company for up to 600 million doses of a coronavirus vaccine.” Under the arrangement, the federal government would obtain the first 100 million doses for \$1.95 billion, with the rights to acquire up to 500 million more. Americans would receive the vaccine for free. Before it could be distributed, it would first need at least emergency approval by the Food and Drug Administration.

See <https://www.nytimes.com/2020/07/22/us/politics/pfizer-gets-1-95-billion-to-produce-coronavirus-vaccine-by-years-end.html>

Pfizer Vaccine: mRNA – BNT162

Age of Study Participants in Phase I and II: 18–55 years of age.

Side Effects Shown in Phases I and II: Mild to moderate symptoms that resolved during the course of the research study.

Dose: Injection of an initial dose followed by a second dose 28 days later.

Predicted Use: Provided all goes well with Pfizer’s Phase III study, Pfizer hopes to have approval by as early as October of 2020.

Availability: If approved, Pfizer expects to manufacture up to 100 million doses of the vaccine by the end of 2020 and 1.3 billion doses by the end of 2021 as of July 22, 2020, by a two billion dollar offer by Trump for Pfizer. In addition, Pfizer and BioNTech announced an agreement with the United Kingdom for 30 Million Doses of mRNA-based Vaccine Candidate against SARS-CoV-2 subject to regulatory approval.

Moderna, Inc., a Biotechnology Company.

Moderna was the first American company to begin a Phase 1 and Phase II trial for a COVID-19 vaccine.

A preliminary report of Moderna’s Phase I clinical vaccine results was published in *The New England Journal of Medicine* on July 14, 2020. Two vaccine injections were provided 28 days apart in 45 healthy adults 18 to 55 years of age. Although there were some local

and systemic adverse effects, these adverse effects were mild to moderate and not severe. See <https://www.nejm.org/doi/full/10.1056/NEJMoa2022483>

Moderna, like Pfizer, uses messenger RNA to target antigens, which results in the vaccine producing antibodies in the human subjects that halt COVID-19 infections. After its Phase II study, Moderna announced that every human subject that received its vaccine developed an immune response to COVID-19.

Moderna originally planned to begin its Phase III trial in mid-July 2020, it recently postponed its Phase III trial to begin July 27, 2020 possibly due to protocol issues with the FDA. For its Phase III trial Moderna in partnership with the National Institutes of Health (NIH)'s National Institute of Allergy and Infectious Diseases (NIAID) has enrolled approximately 30,000 participants in the United States.

Moderna states it hopes to begin its Phase III trial on July 27, 2020 and if it goes well, it expects to have approval to begin providing vaccination early in 2021.

Moderna Vaccine: mRNA-1273

Age of Study Participants in Phase I and II: 18 – 55 years of age.

Side Effects Shown in Phases I and II: Mild to moderate complaints that resolved during the course of the research study. No serious adverse effects were reported through day 57 of Phase II.

Dose: Injection of an initial dose followed by a second dose 28 days later.

Predicted Use: Provided all goes well in Moderna's Phase III study, Moderna hopes to have approval and begin providing the vaccine in early 2021.

Availability: Moderna is aiming for one billion vaccination injections a year doses of the vaccine could be manufactured following approval. Moderna has partnered with Lonza manufacturing to increase production of the vaccine.

<https://www.fiercepharma.com/manufacturing/moderna-aims-for-a-billion-covid-19-shots-a-year-lonza-manufacturing-tie-up>

In summary, the long and short of this vaccine discussion is HOPE – hope that this social isolation, suffering and loss of beloved family and friends due to the Pandemic may end.

Hopefully, if the end of the Pandemic is in sight, we will all remember, continue to learn and take action to make permanent changes related to racial equity, economic equity, the environment and all other critical issues related to our world's emotional and physical health.

