Public Health
Seattle & King County

**Frequently Asked Questions about COVID-19 Vaccination**

First and foremost, questions are a good thing. We expect that smart, concerned persons will naturally want to know more about the vaccine to understand the benefits and risks. Below we detail some of the questions highlighted by EMS and Fire personnel. In addition, there are some excellent resources provided by the CDC and FDA at the end of this document.

**1. The vaccines use messenger RNA or "mRNA" to activate the immune system. This approach is new for vaccination. What do we know about the science of this approach?**

Although vaccine use of mRNA is new, the science and technology involving mRNA is well-established and well-studied. Here are a few basic facts about how the mRNA vaccine works:

- Our bodies produce and use mRNA to make proteins all the time. mRNA is essential to generating an immune response. The mRNA vaccine is taking advantage of the scientific understanding of how our immune systems naturally function.
- The mRNA vaccine does not use active virus, and so there is no chance that the vaccine can transmit COVID.
- The mRNA vaccine does not change the cells' master plan – information that is maintained by the nucleus and its DNA. In fact, the mRNA never enters the nucleus and cannot change genetic code. Rather, the mRNA harnesses the body's existing machinery to help produce antibodies.
- The mRNA – like its name – messages the muscle cells (where it is injected) to produce a small protein that is part of the virus shell. In this case, the protein is part of the "spike". The COVID virus uses that spike to latch onto cells to produce an infection. After vaccination, our body produces this fragment (without any other parts of the virus) and activates the immune system. The immune system makes antibodies against the spike protein that stand-at-the-ready if we later encounter the real COVID virus.
- After providing instructions to make the spike protein, the vaccine mRNA is broken down using the same processes that our bodies use to breakdown our own mRNA. Thus, mRNA does not linger once its mission to make the spike protein is accomplished.

**2. The development of prior vaccines took longer. The new COVID vaccines were developed in less than a year. How was the vaccine developed so rapidly?**

- As a global emergency, the COVID pandemic activated multiple vaccine stakeholders to focus all their energies with great urgency to solve this challenge. The remarkable collection of brainpower, technology, and financial support provided the very best motivation and mix to accelerate the science. With this collective, there was both collaboration and competition that positively moved the process ahead.
- The scientific community just knows much more now than with prior new vaccines. We started with better technology to design vaccines. Indeed, mRNA vaccine technology has been in development for other vaccines. This work quickly pivoted to concentrate of SARS-Cov-2 at the outset of the pandemic. With regard to understanding the virus itself, the SARS event in 2003 produced substantial research that advanced our understanding of how the coronaviruses cause initial infection and disease.
- Evaluation of vaccine candidates and planning to produce the vaccine happened at about the same time instead of in sequence. Often there are months or even years between the completion of one phase and launch of the next phase of vaccination testing (see below for a description of the phases of testing). For

COVID however, planners were considering the infrastructure and design for the next phase during the earlier phase, so that there was no delay progressing to the next phase of evaluation. As the vaccine was being tested, vaccine production also began such that production and distribution processes are all in place.

- Finally, clinical trials have benefitted greatly from modern technology. Collection of information about the people participating in the clinical trial, including their illnesses and potential side effects, was greatly aided by electronic communication tools compared to paper forms used in the past. The statistical analysis could be performed rapidly, and results are disseminated widely within weeks instead of months.

**3. What is the process for a vaccine to be approved and be available to the public?**

Importantly, there were no "shortcuts" in developing or manufacturing these vaccines. The COVID vaccines have followed all the normal steps or "phases" necessary for scientific best-practices in vaccine development.

- First, a vaccine is developed in the lab and evaluated in animals.
- *Phase 1.* If it appears safe and produces the right immune response, then the vaccine is tested in a small group of human volunteers. In a phase 1 study, there is close monitoring of the handful of persons who receive the vaccine (typically 50-100) to evaluate safety and measure the immune response.
- *Phase 2.* If the vaccine passes phase 1 criteria, then it is "trialed" in a larger group of persons (many hundreds). In Phase 2, half of persons receive the real vaccine and the other half placebo (injection of saline). The Phase 2 study evaluates symptoms and immune response and compares these measures between the vaccine and the placebo. Participants in phase 2 studies are carefully monitored for side effects. If the phase 2 study demonstrates good safety and promising immune responses, the vaccine enters Phase 3.
- *Phase 3.* Finally, the vaccine is tested in tens of thousands of persons who are randomly assigned to receive either the vaccine or the placebo. During Phase 3, neither the participants nor the frontline researchers know who has been given vaccine or placebo. The study team closely monitors participants for several months to understand who is infected with COVID and what types of side effects have occurred. An independent, third party group without ties to the company or the frontline researchers has the link to know who received real vaccine or placebo. At the end of the study, the statisticians analyze the data; and then the link between participant and their treatment arm (vaccine or placebo) is revealed.
- This study design, termed a placebo-controlled, double blinded study – guards against any bias. This rigorous study design assures an objective assessment of clinical effectiveness and safety of the vaccine. Throughout, the FDA requires strict adherence to the study protocol. This approach is the gold-standard for scientific evaluation. The FDA-approved vaccines all adhere to this gold-standard approach.
- The results of the studies are then reviewed by another independent group Advisory Committee on Immunization Practices (ACIP). The ACIP is comprised of a wide range of experts and persons from the lay public and reviews all the information and makes a recommendation to the FDA regarding approval. As with all vaccines, even after FDA approval, there are planned efforts to continue to monitor effectiveness and potential for side effects during a Phase 4 effort.

**4. How effective are the FDA-approved vaccines?**

The two mRA vaccines by Pfizer / BioNTech and Moderna are exceptionally effective. In the Pfizer study for example, there were 170 clinical COVID infections in which patients became sick and testing confirmed COVID.

Among these 170 clinical infections, 162 (or 95%) occurred in the placebo group and only 8 (5%) occurred in the active vaccination arm.

This level of effectiveness is outstanding and far exceeds the FDA requirements that are used for most vaccines. Importantly the vaccine is similarly quite effective across a range of subgroups. *For example, the vaccine was more than 90% effective regardless of sex, age, race, or chronic health conditions*. The vaccine had benefit regardless of which demographic or clinical subgroup that describes you.

**5. The approved vaccines require a two-shot series. Do you need to receive the same "brand" of vaccine for both shots?**

With the Pfizer / BioNTech product, the initial vaccination is followed about 3 weeks later with a second shot. With Moderna vaccine, the initial shot is followed 4-5 weeks later with the second shot. You cannot mix and match. The second shot in the series must be the same "brand" as the initial vaccine.

**6. What types of side effects occur with the vaccine?**

Both the Pfizer / BioNTech and Moderna vaccines are exceptionally safe. Most side effects and safety concerns occur within the first few days after vaccination, and the studies evaluated safety particularly for the initial 8 weeks after vaccination with follow-up ongoing. The randomized study design enables us to compare the likelihood of immunity-related symptoms, complications, and other side effects between those who received the real vaccine and those who received the placebo.

*Deaths.* The Pfizer / BioNTech vaccine was not associated with an increase in serious adverse events. More than 40,000 people were enrolled in the study and more than 20,000 received active vaccine. Importantly, there were no deaths attributable to the vaccine. Two people who received real vaccine died compared to four people who received placebo. The causes of death in the vaccination and placebo group were not related to immune causes. The study staff is continuing to monitor subjects for deaths.

*Serious adverse events*. There was no difference between the active vaccination or the placebo in the risk of serious adverse events such as stroke or heart attack. In the Pfizer study, the risk of a serious adverse event was about 1 in 200 for both the active vaccination and the placebo arm – indicating no serious specific risk related to the vaccine.

*Transient symptoms and side effects.* In the Pfizer study, symptoms like injection site soreness, body aches, and fatigue were common in the first day or two after vaccination. This symptom resolved on its own, typically in a couple of days.

The active vaccine caused transient symptoms more often than the placebo injection. *Keep in mind that the expectation from the researchers was that the vaccination group should experience a higher rate of transient symptoms as the immune system responds to the activation of the vaccine.*

*1st dose versus 2nd dose*. Transient symptoms were more common after the second dose of vaccine than the first dose. Again, this type of response after the second shot was expected as the immune system is primed by the first dose of vaccine.

*Injection site soreness.* The most common symptom was soreness at the injection site which occurred much more often in the active vaccine where about three quarters experienced mild to moderate soreness at the injection site compared to only about 10% in the placebo group.

*Systemic symptoms.* The group receiving the active vaccine was also more likely to experience fatigue, headache, and body aches. For example, about half of participants in the active vaccine group noted mild-moderate fatigue compared to about a quarter of participants in the placebo group. These side effect symptoms were more likely to occur in those <55 years of age compared to those >55 years.

*Fever.* One hallmark sign of immune response and vaccine reaction is fever. Fever as defined as a temperature of at least 38.0 C (100.4 F). Like the other symptoms and side effects, fever occurred more often in the vaccination arm and was clearly related to the dose sequence. With the first dose, fever was uncommon: ~2% in the vaccine group versus 0.5% in the placebo group. Following the second dose, fever occurred in about 13% of the vaccine group versus 0.5% in the placebo group. Fever was more common in persons <55 years compared to >55 years. For example, fever occurred after the second dose of vaccine in 16% of those <55 versus 11% > 55.

These side effect symptoms related to the vaccine including fever were almost always mild to moderate and always resolved, typically in a couple of days.

**7. What if I have already had COVID-19, do I need a vaccine?**

"Yes" is the short answer. The recommendation from the CDC and other health experts is you should receive the vaccine even if you have had COVID-19. The vaccine appears to have advantages. "Natural immunity" that comes from the infection may start to wane beginning as soon as a few months after the infection. In contrast, the vaccine's immune response appears to outpace what occurs following a COVID-19 infection, at least hinting that the protection may be superior and last longer. Of course, there is more to learn, but this is an encouraging finding. The CDC does provide the option for someone who has been infected in the past 90 days to defer to others in their vaccination group, but the general recommendation is to receive vaccine regardless of your prior infection status.

The CDC provides this perspective on the topic:

> *Healthcare professionals with documented acute SARS-CoV-2 infection in the preceding 90 days may choose to delay vaccination until near the end of the 90 day period in order to facilitate vaccination of those HCP who remain susceptible to infection, as current evidence suggests reinfection is uncommon during this period after initial infection.*

**8. Will vaccination mean I no longer have to undertake all the other practices to prevent COVID-19 transmission (masking, distancing, hygiene)?**

For now, people who have been vaccinated still need to continue all of the other practices to prevent COVID-19 transmission, including the 3 W's: **W**ear a mask, **W**ash your hands, and **W**atch your distance. The vaccine is 95%, but not 100%, effective. The clinical trial did not measure infectivity. No one yet knows how many people who have been vaccinated may still spread COVID-19 to others while having no symptoms. Studies are ongoing to understand if, how, and when vaccination affects disease transmission and how we may be able to modify current practices. Without vaccination however, we will not be able to consider this potential for change.

**Additional Resources**

https://www.cdc.gov/vaccines/covid-19/health-systems-communication-toolkit.html

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/mrna.html

https://www.fda.gov/vaccines-blood-biologics/development-approval-process-cber/vaccine-development-101