

## COVID-19 Vaccine Advisory from the National MPS Society

We have received several requests for information on the Pfizer-BioNTech and Moderna mRNA-based COVID-19 vaccines that have recently been approved with an Emergency Use Authorization (EUA) from the FDA. These vaccines are currently being shipped around the country and being administered to first tier priority recipients. Based on the presented vaccine clinical trial data, the independent external review, and the FDA granting of an EUA, these vaccines are judged safe and effective. An excellent CDC online slide deck is available ([click here](#)) and covers many of the issues specific to the Pfizer-BioNTech vaccine in more detail as well as issues not covered in the FAQs below. If something is not covered below, please bring these questions to the National MPS Society's Chief Scientific Officer through the [Society's Science Question Portal](#).

The Society advises that all patients/guardians make decisions in conjunction with their medical providers and does not provide specific recommendations. However, healthcare information is often complex and difficult to decipher. Below are answers to some common questions to help you navigate this often-challenging landscape.

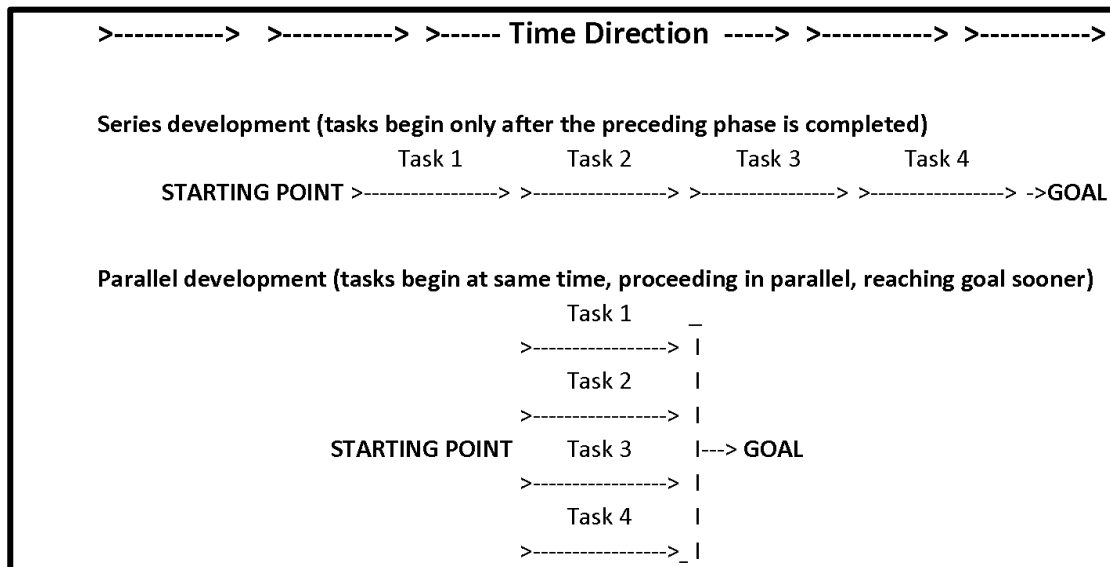
### Frequently asked questions about COVID-19

1. I have heard of both COVID-19 as well as SARS-CoV-2. What is the difference between these two things? Are they the same thing? If not, how are they related?
  - a. One is a disease (COVID-19) and one is the virus that causes that disease (SARS-CoV-2). The term COVID, is often used interchangeably for both.
  - b. The disease we are seeing during this current pandemic is called COVID-19 (short for **Corona Virus Disease 2019**) and refers to a life-threatening disease first seen in 2019 caused by a novel (new) coronavirus
  - c. This newly discovered virus is very closely related at the genetic sequence level (the virus' genome) to the same virus that caused the 2003 SARS outbreak. Because this is the second disease-causing coronavirus that is closely related to SARS, the name of the virus is SARS-CoV-2 for SARS coronavirus 2. The virus is easily spread via a respiratory route and is currently the cause of a worldwide pandemic. The rate of spread in the USA is increasing in all regions. Recently a mutant strain has arisen that spreads more easily, underscoring the need to adhere to continual public health efforts.
2. These vaccines worry me. I am not sure they have been well-tested. How safe are they?
  - a. The Pfizer-BioNTech vaccine against COVID-19 has been evaluated in over 43,000 participants and the Moderna vaccine in over 30,000 people.
    - i. Details for the vaccines and the testing details can be found here:
      1. [Pfizer/BioNTech](#)
      2. [Moderna](#)
  - b. The vaccines were found to be safe. The reactions to the vaccine are divided into local (around the site of injections), systemic (whole body symptoms), and severe adverse events. The vaccines led to minor local and systemic reactions as would be expected for any vaccine. Following are links to the extremely well-detailed evidence on safety for the two vaccines broken down by age, symptom, and dose, comparing those vaccinated with the vaccine versus placebo:
    - i. [Safety details of the Pfizer-BioNTech vaccine clinical trial data.](#)
    - ii. [Safety details of the Moderna vaccine clinical trial data.](#)

3. How effective is it?
  - a. In the [Pfizer-BioNTech study](#), there were a total of 170 cases of COVID-19 seen: 162 (95%) in the unvaccinated (placebo) group, and 8 (5%) in the vaccinated group. This is where the number of a 95% effective COVID-19 disease prevention comes from ( $162/170 = 95\%$ ).
  - b. In the [Moderna study](#), there were 196 infections seen: 185 (94%) in the unvaccinated (placebo) group, and 11 (6%) in the vaccinated group. This is where the number of a 94% effective COVID-19 disease prevention comes from ( $185/196 = 94\%$ ).
  - c. Additionally, the vaccines appear to prevent serious disease (that which may require hospitalization). In the Pfizer-BioNTech study there were 10 serious cases of COVID-19 seen: nine in the unvaccinated (placebo) group, with only one case in the vaccinated group. In the Moderna study there were 30 cases of severe COVID-19, all within the placebo group.
  
4. How well will the vaccine work on an older person, or someone of a diverse background or with predisposing conditions?
  - a. The vaccine appears equally effective across age (adults 16 or older for the Pfizer-BioNTech vaccine and over 18 for the Moderna vaccine), gender, race, ethnicity, and demographic considerations. The details of the trial participants can be found below.
    - i. Demographics of the Pfizer-BioNTech vaccine trial participants is in [Table 1 of the New England Journal of Medicine publication](#).
      1. Over 42% of participants were over the age of 55
      2. While some individual groups are not heavily represented, over 44% of participants were from diverse backgrounds including Black/African American (9.3%), Asian (4.3%), Native American/Alaska Native (0.5%), Native Hawaiian/Pacific Islander (0.2%), Multiracial (2.3%), and Hispanic/Latinx (28%).
    - ii. Demographics of the Moderna Vaccine trial participants can be found [at this provided link](#)
      1. Over 25% of participants were over 65
      2. Overall, 37% of participants came from diverse backgrounds including Black/African American (10%), Asian (4%), Hispanic/Latinx (20%), and other backgrounds (3%).
  
5. I'm worried about side effects. What kind of side effects were there?
  - a. The side effects noted in the clinical trials were minor (including local reactions of pain and swelling as well as systemic reactions including headache, fatigue, muscle and joint aches, fever, etc.), lasting only a day or two, and are consistent with what is seen with other vaccines. These are normal and anticipated side effects of a vaccination, and are signs of your immune response reacting, which is the objective of a vaccination.
    - i. The [details for the Pfizer-BioNTech vaccine can be found here](#).
      1. In people aged 18-55:
        - a. Fever or chills were seen only rarely in the placebo group and in between 15-36% of individuals after the second inoculation versus 3-14% after the first inoculation. This pattern of fever was seen in people over 55 but overall, less often.
        - b. Fatigue or headache were seen commonly in the placebo group (22-34%), were seen at increased rates in the vaccinated group (41-60%), with higher rates for fatigue, and overall higher rates of both symptoms after the second inoculation. This same overall pattern of symptoms was seen in people over 55 but at overall reduced frequency.

- c. New or worsening muscle or joint pain were seen commonly in the placebo group (5-10%), were seen at increased rates in the vaccinated group (11-38%), with higher rates for muscle pain, and overall higher rates of both symptoms after the second inoculation. This same overall pattern of symptoms was seen in people over 55 but at overall reduced frequency.
      - d. Gastrointestinal signs were seen in both groups but without any clear pattern of difference between the placebo and vaccinated participants. Diarrhea was reported in between 8-12% of all participants after all doses, and vomiting was reported in 1-2% of all participants after all doses. Rare cases of severe dehydration (requiring intravenous fluids) from diarrhea or vomiting were seen in up to 1-4 participants (less than 0.2%) from both placebo and vaccinated groups, and after both inoculations.
    - ii. The general trend for the [local and system reactions to the Moderna vaccine](#) is very similar.
6. How many shots/jabs do I need to get to be protected?
- a. The vaccines require a first dose and a booster 21-28 days after the first vaccine.
    - i. The time between injections is based on whether you receive the Pfizer-BioNTech (21 days) or the Moderna (8 days) vaccine.
    - ii. Other vaccines in development but not yet approved may only require one inoculation.
7. I'm worried that the vaccine might give me COVID-19.
- a. That is not possible because the vaccine does not contain any SARS-CoV-2 virus, which is the virus that causes COVID-19. The Pfizer-BioNTech and Moderna vaccines only contain mRNA for one component of the virus.
  - b. As a result, it is impossible for a person vaccinated with the vaccines to "get the virus" from the vaccine.
8. I am hoping to get involved in a future AAV-based gene therapy trial. Will this vaccine interfere with any possible AAV based trial?
- a. AAV vector-based gene therapy trials will use one of many AAV surface proteins in their vectors. If you have a pre-existing antibody response to the particular surface protein (capsid protein in the parlance of AAV vectors) being used, you will usually be excluded from that trial. Because the Pfizer-BioNTech vaccine, the Moderna vaccine, and all other vaccines in the Warp Speed development group will not use AAV-based vectors, these vaccines should be entirely safe in this respect, and consistent with any past or pending AAV viral vector clinical trial. None of these vaccines use AAV-based viral vectors, so they should present no risk to past or pending AAV-based trial participation. There are some AAV-based vectors in the pipeline with some companies, but these are not yet in clinical trials, so it is not a near-term concern.
9. I am someone (or care for someone) who has had a bone marrow transplant (BMT) or hematopoietic stem cell transplant (HSCT). Is the vaccine safe for this group?
- a. For the specific issue of a BMT or HSCT patient over 16 and whether to vaccinate or not, this is a decision that one needs to arrive at with their clinician.
  - b. However, a stable and successfully transplanted patient has a normal (non-MPS) immune system to the degree that the cells of the transplant are the cell types involved in the response to a vaccine.
  - c. If you or your MPS child receive normal childhood/adult vaccines, this suggests your clinician considers the immune system to be immunocompetent (able to respond to vaccination).

10. What if a person is on immunosuppressive therapy?
- None of the vaccines (including the currently approved Pfizer-BioNTech vaccine) approved or under development as part of the Warp Speed program in the U.S. contain live virus or viral vectors capable of replicating, so individuals currently on immunosuppressive therapy should be able to safely receive vaccines, *if otherwise cleared by their care provider*. Because immunosuppressive therapy may limit their immune response to a vaccine, patients should confer with their care providers regarding precautions to avoid further exposure to the novel coronavirus. The CDC has an excellent fact sheet [about immunosuppressed patients here, including detailed information on many other conditions and how it may affect vaccination recommendations](#).
11. The whole Warp Speed thing worries me. I want a safe vaccine not something from Star Trek.
- It is important to remember that the US Federal program referred to as Warp Speed, was focused on a vaccine that was produced safely and adhered to all safety requirements of the FDA.
  - Development was both quick and safe for the following reasons:
    - The mRNA technology can advance quickly based on just the viral genome sequence, which became known just in January (January 10, 2020, to be exact).
    - The Warp Speed process of the government reduced economic risk to companies and streamlined certain aspects of the regulatory process, so they could advance based on medical safety and science and not economics and bureaucracy.
  - All of the same safety measures and trials that would be met under ordinary regulatory provisions have been met under the Warp Speed program
  - The Warp Speed regulatory efficiency involved streamlining, with production proceeding “in series” rather than “in parallel”. See the info graphic below:
  - Funds from the Warp Speed program allow companies to pursue many of the needed aspects of production and testing simultaneously, rather than one after another, allowing for faster development. This is another aspect of “in parallel” versus “in series” development.



12. When can my child receive a vaccine?
- At this point, none of the current vaccines have been evaluated yet in children so the vaccine recommendations are only for people over 16 years of age (Pfizer-BioNTech vaccine) or 18 years of age

(Moderna/NIH vaccine). So, if your child is not yet old enough, they are not eligible to receive any of the currently approved vaccines. At least 3 vaccines (Pfizer-BioNTech, Moderna, and AstraZeneca) have been approved for or begun clinical trials in children 12 years and older, but the results are incomplete and none have been approved for children yet.

13. When will an MPS patient be eligible for a vaccine?
  - a. Most of our MPS patients could be considered to be in the CDCs category 1C in their priority scheme, as they have an underlying medical concern, many involving multiple cardiac and respiratory issues, that could reasonably place them in this category.
  
14. I know an MPS patient that is in the CDC priority category 1C but they are not yet eligible for a vaccine in my state. Why is that?
  - a. It is important to remember that the CDC recommendations may be substantially altered by state medical or public health entities that are actually charged with overseeing the vaccine rollout in their states. Therefore, you will need to check with your own state/county. But for those who are interested, here is a link to the CDC site for "[Vaccination Considerations for Persons with Underlying Medical Conditions](#)".
  
15. I have heard that these vaccines are mRNA vaccines and that they have never been used before? What is mRNA and what is an mRNA vaccine?
  - a. The vaccines from Pfizer-BioNTech and Moderna are based on and contain a type of genetic material called mRNA (short for messenger ribonucleic acid). In fact, mRNA is part of every living thing more complicated than bacteria (which have RNA but not exactly the same type as humans have).
  - b. All of our metabolically active cells are chock full of their own mRNA. Every protein in our bodies started out as an mRNA molecule that was the "message" (hence the term mRNA) that was translated to a peptide (protein) sequence.
  - c. The mRNA-based type vaccines have been under development as an approach for some time, and that is why the technology advanced so quickly for the COVID-19 vaccine.
  - d. The vaccines are stored at low temperature (sometimes very low temperature in the case of the Pfizer-BioNTech) because mRNA is easily degraded.
  - e. The mRNA in the vaccine contains the coded genetic sequence for the viral "spike" protein.
  - f. The coronavirus spike protein helps get the virus into our cells and start an infection.
  - g. The mRNA in the vaccines leads cells in your body to produce the spike protein, which the body recognizes as a foreign protein, thus causing an immune response to the spike protein.
  - h. The vaccine response against the spike protein prevents 95% of clinical infections.
  - i. There is nothing dangerous about mRNA. It is a normal part of living cells. We all make a lot of our own mRNA in every one of our own cells. All of the different proteins in our bodies were produced based on the specific genetic codes of our own mRNA.
  - j. The mRNA in the vaccine is the same generic type of genetic material in our own cells, except that it codes for the genetic sequence of the viral spike protein.
  - k. The vaccine mRNA will not in any way interfere with a person's own genetic material (DNA), a particular MPS disease causing mutation, or genome.
  - l. The mRNA in the vaccine has been mass produced so that it can be packaged into a vaccine, but otherwise it is the same mRNA that would be produced in our cells from a naturally acquired infection with the virus.

16. Are the mRNA-based vaccines safe? They were developed so fast. It sounds scary to have genetic material injected.
- a. The CDC has a great description of mRNA vaccines that is very helpful and can be found [here](#).
  - b. The mRNA in the vaccine does not affect or interact with our DNA in any way.
  - c. The mRNA in the vaccine never enters the nucleus of the cell, which is where our DNA (genetic material) resides.
  - d. Our cell breaks down and gets rid of the mRNA from the vaccine soon after it is finished using the instructions, in the same way that our bodies' cells break down their own mRNA.
  - e. The mRNA vaccines contain the SARS-CoV-2 mRNA sequence for only the viral spike protein. An immune response that is successfully directed against this protein, will limit the ability of any virus a person is exposed to, to enter a cell and cause an infection.
  - f. By exposing us to just the mRNA of the spike protein, the vaccine delivers to our immune system the same type of exposure to the spike protein as an actual viral infection, without exposing us to the virus and all the potential for illness and death that comes with a case of COVID-19.
  - g. The mRNA vaccines can never give someone COVID-19, because mRNA vaccines do not use the live virus that causes COVID-19. In that regard they are considered a safe option. There is zero chance you could get COVID-19 from these mRNA vaccinations and based on the clinical trial data, there is a 95% benefit in terms of being protected from getting COVID-19, as well as being protected from serious COVID-19 disease if you are unlucky enough to be in the 5% that is not fully protected by the vaccine.
  - h. It may be helpful to remember that all vaccines based on viruses and bacteria have genetic material. The genetic material is just part of the organism that is being delivered in the vaccine (exceptions are the vaccines based on purified antigens or toxoids, an example of the latter being vaccines for tetanus and diphtheria that contain inactive proteins (toxoids)). The mRNA vaccines have just gone to the logical step of delivering the mRNA and sidestepping other parts of an organism. There are many arguments that can be made that this approach makes mRNA vaccines safer in some respects.
17. In conclusion, when you consider the following, a serious consideration on vaccination should be contemplated and discussed with one's primary care provider.
- a. An MPS patient may be at increased risk for severe COVID-19 disease.
  - b. A successfully transplanted patient may be considered immunocompetent with a full and stable transplant engraftment.
  - c. The current vaccines have no potential to cause viral disease (such as COVID) because they contain no virus.
  - d. The current clinical trials' efficacy and safety data was good enough to lead to a recommendation to approve an Emergency Use Authorization by an outside independent panel, which was subsequently adopted by the FDA.