INFORMED CONSENT FORM
AND
AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**Division of Microbiology and Infectious Diseases (DMID), National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) / "Phase 2 Clinical Trial to Optimize Immune Coverage of SARS-CoV-2 Existing and Emerging Variants"**
Protocol Number:	**22-0004**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

KEY INFORMATION

You are being asked to take part in this study because we would like to know if giving additional doses of the original vaccines against SARS-CoV-2 (the virus that causes COVID-19) or experimental versions of these vaccines with different variant strains are safe and how they may affect the immune system.

- Being in the study is voluntary – it is your choice.
- Your participation in this study will last for about 12 to 24 months.
- Procedures will include collection of health information, injections, blood draws, and potentially a nasal swab of your nose.
- There are risks from participating.
    - The most common risk is pain at the site of injection.
    - One of the most serious risks is anaphylaxis, or severe allergic reaction to the study vaccine. See the "Risks of Participation" section in this consent form for more information. You should discuss these risks in detail with the study team.
    - There is risk of loss of confidentiality of your health information.
- You might not benefit from being in this research study. There may be benefit to getting a second booster of the original vaccine against SARS-CoV-2 if you are an adult 50 years or older, but we do not know whether vaccines based on the new variants will offer benefit.
- As part of this study, we are obtaining extra blood samples from you, and one to two nasal swabs if you have symptoms consistent with COVID-19 or test positive for COVID-19 outside of the study. We will use your coded information, leftover samples, and extra

samples for **secondary research** (the research is not planned yet). It will include **genetic** research. When you give consent, you will take part in the vaccine study and allow for secondary research.

Please read this form carefully. Take your time to ask the study doctor or study staff as many questions about the study as you would like. The study doctor or study staff can explain words or information that you do not understand. Reading this form and talking to the study doctor or study staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form and date it.

BACKGROUND

The purpose of this study is to learn about the safety and immunogenicity (ability to provoke an immune response, which can indicate how well a vaccine works) of booster vaccines to SARS-CoV-2. Multiple SARS-CoV-2 vaccines have been studied in large studies with tens of thousands of participants, and have been granted either Emergency Use Authorization (EUA) or approval by the United States Food and Drug Administration (FDA) and are being used in the national COVID-19 vaccination campaign. All the current vaccines approved or authorized under EUA deliver the spike protein (the protein that allows the virus to enter human cells) to the immune system to generate immunity to that specific viral protein.

Messenger ribonucleic acid (**mRNA**) vaccines include the genetic code of the spike protein. Moderna and Pfizer/BioNTech have both received FDA approval for a vaccine using this strategy that is given as a two-dose primary series. **Adenovirus** vaccines use defective adenoviruses (common cold viruses that cannot grow) carrying the code for spike protein inside the viral particles, delivering the instructions to make the spike protein. Johnson & Johnson in partnership with Janssen has received EUA in the U.S. for a vaccine using a human adenovirus 26 (Ad26) vector in 2020. The Johnson & Johnson vaccine primary series is a single dose vaccine. Additionally, Sanofi-GSK has developed a third vaccine type, **an adjuvanted recombinant protein subunit** vaccine, which contains copies of the spike protein itself with an adjuvant. Adjuvants are ingredients added to help a vaccine work better by increasing the immune response. The adjuvant in the Sanofi-GSK vaccine is called AS03. The Sanofi-GSK vaccine is still considered experimental but has been tested in a phase 3 clinical trial and shown to be effective in protecting against COVID-19 and Sanofi-GSK is in the process of applying for FDA EUA.

Since EUA of the Moderna, Pfizer and Johnson & Johnson vaccines, billions of people around the world have since been vaccinated against symptomatic COVID-19 and severe disease. In further study, scientists and researchers have found that the protection against COVID-19 provided by these vaccines wanes over time and additional doses may be needed to continue to prevent COVID-19. The FDA gave EUA for a booster dose (3rd doses of Moderna or Pfizer/BioNTech and a 2nd dose of Johnson & Johnson) in Fall 2021 and the Centers for Disease Control and Prevention (CDC) now recommends that all adults receive booster doses at least 2 months after a primary Johnson & Johnson vaccine or at least 5 months after the second dose of Moderna or Pfizer/BioNTech.

Additionally, the FDA has now expanded the EUA for Moderna and Pfizer for a second booster at least 4 months from the last dose for adults 50 years and older. The CDC guidance also now allows for second booster dose to be given to adults 50 years and older who, based on age or medical history, continue to be at risk for serious COVID-19 illnesses and those who received 2 doses of the Johnson & Johnson vaccine.

However, current primary and booster doses of all three vaccines deliver spike protein based on the strain of the virus from early 2020, and the spike protein over the course of the pandemic continues to change with ongoing circulation of the virus. These changes have led to new strains, also called variants, which continue to cause surges of new cases around the world. It's possible that updated variant versions of the vaccines will be needed in the future. Booster vaccines using updated spike proteins to reflect the circulating variants, or using different vaccine delivery types, may improve the immune response to prevent infection longer, more effectively, or from more variants.

The remaining sections describe more about the research study. Members of the study team will talk with you about the information in this document. You are encouraged to ask any questions and discuss this study with family, friends, and anyone you choose. If you decide to take part in this study, you will be asked to sign and date this consent form. A copy of this signed and dated consent will be given to you to keep. Signing and dating this consent form indicates that you understand your involvement in the study, the risks of participating and that you agree to take part in the study.

PURPOSE OF THIS RESEARCH STUDY

The purpose of this research is to test additional vaccine booster shots that use different vaccine types and/or variant spikes to see if these new combinations are safe and to evaluate the immune system responses. Vaccines tell your germ-fighting cells to make antibodies and other substances to fight infections. All the study vaccines are intended to train the immune system so that if the person is then infected with the SARS-CoV-2 virus, they have a "head start" and the infection can be stopped or made less severe. Based on what we know, we would anticipate any of the vaccines used in this study to boost antibodies and provide similar protection as if you received a second booster dose of the original vaccine. However, using a booster vaccine that has one or more different variant spikes, or the original spike in combination with variant spikes, may improve protection against variant strains.

This study uses vaccines that have received FDA approval or EUA and also experimental vaccines that are still under investigation. The vaccines used in this study include different vaccine types, the variant spikes, or both together as experimental vaccine approaches.

Experimental means the study vaccine is not approved for routine use by the FDA; however, the FDA is allowing experimental variant vaccines to be used that have been developed in the same manner as approved vaccines. Some of the vaccines used in this study may include:

- A low dose Moderna vaccine, mRNA-1273, 50 mcg, granted FDA EUA as a booster

- Moderna mRNA study vaccines updated with three new variants: B.1.351 (Beta variant), B.1.617.2 (Delta variant) and B.1.1.519 (Omicron variant)
- Moderna mRNA study vaccines containing a combination of 2 or more variants
- A Pfizer mRNA vaccine, BNT162b2, 30 mcg, granted FDA EUA as a booster
- Pfizer mRNA vaccines updated with two new variants B.1.351 (Beta variant) and B.1.1.519 (Omicron variant)
- Pfizer mRNA study vaccines containing a combination of 2 or more variants
- A Sanofi-GSK recombinant protein vaccine, CoV2 preS dTM-AS03, 5 mcg dose
- A Sanofi-GSK recombinant protein vaccine updated with the B.1.351 (Beta) variant
- A Sanofi-GSK recombinant protein vaccine containing a combination of 2 variants (2.5 mcg dose for each variant)
- Variant study vaccines using different technologies to deliver spike protein

Groups of participants who have already received the Moderna primary series (2 doses) and booster, the Pfizer primary series (2 doses) and booster, or Janssen vaccine (1 dose) and booster as recommended by the CDC will be enrolled. Immune responses to additional booster doses may also differ based on age and whether or not someone has been infected and recovered from SARS-CoV-2. We have therefore designed the study to have at least 45% of adults aged 65 years or older and 20% of participants who are fully vaccinated and have recovered from COVID-19.

This study will be enrolled in at least 3 stages. We anticipate about 600 individuals will be enrolled in Stage 1 and receive one of the Moderna vaccines as described in Table 1 below which will include mRNA for one or more strains or variants. In Stage 2, we will enroll approximately 300 participants who will receive one of the Pfizer vaccines as described in Table 2 below which will include mRNA for one or more strains or variants. In Stage 3, we will enroll approximately 150 participants who will receive one of the Sanofi-GSK vaccines as described in Table 3 below which will include spike protein for one or more strains or variants. You will not be able to choose to be part of a specific arm (group) or receive a specific study vaccine. This will be randomly assigned. For stage 1, in one arm of the study participants will receive 2 doses at least 8 weeks apart. Because this is an adaptive trial, additional stages and the number of participants to be enrolled, as well as the specific study vaccines to be given in future stages, are still yet to be determined.

Table 1: Stage 1 Study Treatment Arms

Arm	Number of participants	First Study vaccination (Day 1)	Second Study vaccination (day 57)
1	100	Moderna mRNA Prototype Vaccine	NA
2	100	Moderna mRNA Beta/Omicron Vaccine	NA
3	100	Moderna mRNA Beta/Omicron Vaccine	Moderna mRNA Beta/Omicron Vaccine
4	100	Moderna mRNA Delta/Omicron Vaccine	NA
5	100	Moderna mRNA Omicron Vaccine	NA
6	100	Moderna mRNA Prototype/Omicron Vaccine	NA

NA = Not Applicable

Table 1: Stage 2 Study Treatment Arms

Arm	Number of participants	First Study vaccination (Day 1)	Second Study vaccination (day 57)
1	50	Pfizer mRNA Prototype Vaccine	NA
2	50	Pfizer mRNA Beta/Omicron Vaccine	NA
3	50	Pfizer mRNA Omicron Vaccine	NA
4	50	Pfizer mRNA Beta Vaccine	NA
5	50	Pfizer mRNA Prototype/Beta Vaccine	NA
6	50	Pfizer mRNA Prototype/Omicron Vaccine	NA

NA = Not Applicable

Table 2: Stage 3 Study Treatment Arms

Arm	Number of participants	First Study vaccination (Day 1)	Second Study vaccination (day 57)
1	50	Sanofi-GSK Prototype Vaccine	NA
2	50	Sanofi-GSK Beta Vaccine	NA
3	50	Sanofi-GSK Protype/Beta Vaccine	NA

NA = Not Applicable

Most participants will attend 8 or 9 in-person study visits, including an initial screening visit (that may be combined with the first study vaccination visit), one study vaccination visit, and 7 in-person follow-up visits. They will be in the study for up to approximately 13 months, if they have a separate screening visit, or 12 months, if the screening visit is combined with the first study vaccination visit. Study visits may include a physical exam, and all but one (the visit seven days after the study vaccination) will include a blood draw. Participants in Arm 3 of stage 1 will have 12-13 in-person study visits including an initial screening visit (that may be combined with the first study vaccination visit), two study vaccination visits, and 10 in-person follow-up visits.

They will be in the study for up to approximately 15 months, if they have a separate screening visit, or 14 months, if the screening visit is combined with the first study vaccination visit.

SELECTION OF STUDY POPULATION
All stages of the study include adults aged 18 years or older who are in stable state of health. We will screen you for eligibility before performing any further study activities or giving you a study vaccination.

You are **not** eligible for this research study if:

- You have been diagnosed with COVID-19 in the past 4 months
- You have a history of receiving a SARS-CoV-2 plasma antibody infusion or SARS-CoV-2 monoclonal antibody infusion (in the last 90 days)
- You have received non-COVID-19 vaccine (within 28 days prior to the first dose with study vaccine, except for influenza vaccine)
- You have received any experimental vaccine or drug in the past 28 days, OR plan to receive one during your study participation
- You have received an experimental coronavirus vaccine
- You have any serious chronic medical or psychiatric conditions
- You are on certain medications
- You are pregnant or breastfeeding a child
- You have a history of hypersensitivity or a severe allergic reaction to vaccine or to polyethylene glycol (PEG), polysorbate or nanolipid particles which are components of the vaccines
- You have a prior history of myocarditis (inflammation of the heart muscle) or pericarditis (inflammation of the lining outside of the heart) (Stages 1 and 2 only)
- You have any medical condition the study doctor feels would make your participation unsafe

WHAT WILL HAPPEN DURING THE STUDY?
If you are assigned to receive 1 dose of study vaccine, your participation in this study will last approximately 12 months and will include approximately 8 or 9 in-person study visits and 1 phone call. If you receive 2 doses of a vaccine, your participation will be 14 months and will include 12 or 13 in–person study visits and 2 phone calls.

Screening
You will have a Screening Visit to check if you are eligible to enroll in this study. The Screening Visit may be combined with the first study vaccination visit. If it is a separate visit, it will take about 60 minutes and will include:

- Reviewing, signing and dating the consent form
- Collecting information about your medical and mental health history, medications, and vaccination history

- A physical exam if needed
- Checking vital signs (blood pressure, pulse, respiratory [breathing] rate, temperature)
- Measuring height and weight
- For participants of childbearing potential, a urine pregnancy test

General Study Visit Procedures
Study visits that include a study vaccination will generally last about 2-3 hours and other visits will generally last about 30 minutes. The first study vaccination visit may be combined with the screening visit and will include the screening visit procedures. Visits may include:

- Questions about your recent medical history and medications, illnesses or symptoms, and side effects or reactions
- Collecting vital signs (heart rate, blood pressure, temperature) before a study vaccination and at other visits if needed
- Having a physical exam if needed
- Collection of blood samples at almost all of the study clinic visits (and if you can become pregnant, urine for pregnancy testing at each of the vaccination visits)
- Study vaccination or assessment of the site of a previous study vaccination if needed
- Review of symptoms after vaccination during telephone calls

Single Vaccine Arm: The single study vaccination will be given on Day 1.

Two Vaccines Arm: The two study vaccinations will be given on Days 1 and 57.

At the study vaccination visits we will review your medical history to confirm that you are eligible for a study vaccination.

You will receive an injection of the study vaccine in the deltoid (shoulder) muscle of your upper arm at each study vaccination visit. You will stay in the clinic for at least 30 minutes after the study vaccination for study staff to check for any immediate reactions.

We will give you a memory aid (like a diary card), thermometer, and ruler (to measure the size of any redness or swelling at the vaccination site) with instructions to record your temperature and any side effects. At home, you will complete the daily memory aid, beginning on the evening of the day of each study vaccination and continuing daily for the next seven days. About seven days after each study vaccination visit the study staff will call you to check-in and make sure you did not need to see a doctor for any side effects. The memory aid will include contact information should you need to contact the study team. You will be instructed to bring the memory aid with you to your next scheduled clinic visit.

We will ask you to keep track of any unexpected symptoms you develop after being vaccinated. You will be asked to recall these symptoms at your safety phone call visit, approximately 1 week after being vaccinated.

If you become sick or have any reactions after a study vaccination, you should immediately contact the study staff. We may ask you to come to the clinic for an extra study visit. The staff may perform additional research or safety procedures, if needed.

Follow Up Visits
In addition to the study vaccination visits, you will also come to the clinic (or speak with us by phone) for follow up visits as described below. Follow-up visits will take about 30 minutes.

Single Vaccine Arm: Day 4, Day 8 or one week (phone call only), 2 weeks, 4 weeks, 3, 6, 9 and 12 months following vaccination.

Two Vaccine Arm: Day 4, Day 8 or one week (phone call only), 2 weeks, 4 weeks, 2 months and 3 days, 1 week (phone call only), 2 weeks, 4 weeks, 3, 6, 9 and 12 months following the second vaccination.

The study staff will call you periodically during your study participation to check on your health status or to remind you of an upcoming visit or for other reasons. We may also contact you by email or text message when appropriate.

Information about your study participation and study results may be included in your electronic health record. If you have concerns about this or wish to obtain more detail, you should discuss this with the study team.

Unscheduled Visits
You may be asked to come back to the study clinic at other times if needed, for example, if you have a serious reaction to vaccine. The study doctor will determine what activities will be needed after reviewing any symptoms that you are having, which may include drawing your blood and/or performing an electrocardiogram (ECG).

You may also have an unscheduled visit if you develop an illness suspicious for COVID-19 or test positive for COVID-19 outside of the study. At that visit 1-2 nasal samples may be collected.

Laboratory Testing of Specimens
The blood specimens collected from you will be used for research tests of the immune response to the study vaccine. These tests will measure how your body developed an immune response to the study vaccine. We will look at your antibodies, which are proteins that your body uses to fight off the virus. We will also look at how different cells of your immune system help to fight the virus. Finally, we may use some of the blood samples to test for a cardiac marker of inflammation of the heart muscle.

Some of the testing in this study will include genetic testing to see how your cells work to develop immune responses. We will not do genetic tests that check for diseases or biomarkers for cancer. You will not receive the results of the genetic testing.

We will use some samples to develop better ways to test a person's response to the study vaccine. Giving blood samples for the research tests will not benefit you. It may benefit others by leading to new approaches in vaccine development or treatments for coronavirus infection. The results of these tests are useful only for research purposes. **Your individual results will not be available to you or your regular doctor and will not be placed in your medical record.**

Nasal swabs will be used to test for the presence of the virus that causes COVID-19 and, if positive, for genetic sequencing of the virus, allowing us to determine what variant has caused you COVID-19. We will let you know if your COVID-19 test at the study site is positive. Since sequencing may be done weeks or months after collection and processed in batches, we will be unable to share the results of this testing with you.

Blood and nasal swab samples for these research tests may be sent to a central storage facility or sent directly to the research testing laboratories. These samples will not be labeled with your name or initials, or any other information that could readily identify you. These samples will be labeled only with a barcode and a unique tracking number (ID code) to help protect your confidentiality. Staff at the central storage facility and research testing laboratories will not know your identity, or even the study identifier you were assigned. However, the study staff who enrolled you will keep a list in a secure area with your name, contact information and the ID code (called a code key) that can link the samples to you, if needed. Access to the code key is limited to study staff working at the research site where your samples were collected.

We may remove the codes from your information or samples so that we cannot identify you and use these in other research. These de-identified samples may be shared with other researchers without your additional consent.

Leftover and Extra Blood Samples

Some of the blood collected for measuring immune responses to the vaccines may not be needed to do the research tests. **We plan to store and use these leftover samples and your information (identified only by ID codes) for secondary research.** Secondary research is research that is not part of this study but will be performed in the future. You will not be told about the future research.

We will also collect extra blood samples at each visit to store and use for secondary and future research. Secondary and future research will be limited to COVID-19 vaccines and may help us understand how the booster vaccines work or to develop new tests. If you do not want to give leftover and extra samples for future and secondary research, you cannot enroll in this study.

Blood samples will be stored indefinitely at a site determined by the National Institutes of Health (NIH). Leftover and extra blood samples will be labeled only with a barcode and an ID code (not with your name, initials, or any other information that could readily identify you).

These leftover and extra blood samples will be stored with the same confidentiality measures used for the main specimens.

Leftover and extra blood samples may be used in the future for research about this study vaccine and your body's response to this study vaccine. This may include genetic testing. Genetic testing will look at the material in your immune cells that tells each immune cell in your body how to work. Future genetic testing may inform development of COVID-19 vaccines, or be used for studies of coronaviruses. You will not be contacted about the types of future research. The genetic testing is for research purposes only and it will not be able to tell you about relatives, paternity, or country of origin. The genetic research testing done in this study will not tell you about diseases that you may get in the future. We will not give you the results from the genetic research testing.

At any time during this study or after this study is over, extra blood samples may be shared with other study doctors/institutions and used for future and secondary research, including genetic testing. Also, after future genetic testing, the resulting data may be shared with other researchers. We will share your future genetic information through a "closed" database, also called a restricted data repository. NIH gives permission to other researchers to use your future genetic information only for research purposes. To qualify, researchers must receive approval from NIH to access and use the future genetic information. A summary of data from all participants may be shared in an "open" database, also called an unrestricted data repository, but this will not contain your individual data. The risk of anyone identifying you with this information is very unlikely. However, there is still a risk of loss of confidentiality.

Your individual data will not contain information that can easily identify you. It may be possible to identify you with your DNA; however, the researchers must follow rules specifically to not identify you. If you change your mind and want to remove your data from the database, you should contact the research site that collected your data. If possible, your data can be removed for further research. Your data cannot be removed if it has already been used.

Leftover and extra blood samples will be used only for research purposes. This may include reproducing or growing your cells. These blood samples will not be sold or used directly for production of any commercial product. However, the research studies in this study or in the future may lead to identification of antibodies or other treatments that could indirectly lead to a commercial product that protects against viral infection or disease.

Although the results of any future research may be patentable or have commercial profit, you will not receive payment if this happens. You will have no legal or financial interest in any commercial development resulting from any future research.

If these blood samples are tested in the future, the results may be published. You will not be identified in such publication. In other words, the publication will not contain any information about you that would enable someone to determine your identity.

By signing and dating this consent form, you are agreeing to the collection, storage and future research use of your blood samples and information collected for this study. There are no benefits to you in the collection, storage and future research use of your blood samples. Future research tests may benefit others by leading to new approaches in the development of vaccines or treatments for coronavirus infections. The results of any future research testing will be kept confidential in the same way as the results of other testing done for this study. The results of any future research will not be available to you or your regular doctor and will not be placed in your medical record.

You may change your mind about future and secondary research and withdraw consent for the storage and use of your coded samples or information at any time. You will need to contact the study doctor using the contact information listed on page 1 of this form. If you have visits after this, we will stop collecting extra blood.

Your samples will be removed from future use when the vaccine study is completed. Only stored samples with an ID code and not used in this research can be removed or destroyed. Research that has already begun using your specimens cannot be withdrawn. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw the specimens and data.

Ask us if you have questions about how your blood samples may be used.

POTENTIAL RISKS AND DISCOMFORTS

There may be some risks to participation in this study. You may experience one or more of the risks or side effects explained below. You should discuss these with the study doctor or study staff. Many side effects go away shortly if treated, but in some cases, side effects can be serious, long lasting, or permanent. The Moderna mRNA-1273 50 mcg study vaccine and Pfizer BNT162b2 30 mcg study vaccine have been granted EUA by the FDA to be used as a booster dose. All of the other study vaccines will be given under experimental authorization in this study. The Moderna variant vaccines (beta strain, omicron strain and delta strain), either alone or in combination, are experimental and have been given to only a few hundred humans. Similarly, the Pfizer variant vaccines (beta strain and omicron strain), either alone or in combination, are experimental and have been given to only a few hundred humans. There may be risks that we do not know about right now. Side effects may occur more frequently with the booster doses compared with the first vaccine.

The possible risks of participating in this study include those associated with having blood drawn, reactions to the injection, adverse effects (side effects) of the study vaccine(s), having nasal swab(s) collected, and the possibility of a breach of confidentiality.

Having your blood taken can cause pain and may also cause lightheadedness or fainting. The needle stick can cause bruising, which can be prevented or reduced by putting pressure on the

site for a few minutes after the needle is removed. It is possible to get an infection at the site of the needle stick. To reduce the risk of infection after the blood draw or study vaccine injection, the study doctor or study staff will wipe the area clean with alcohol and use sterile equipment. Throughout this study, the amount of blood collected will not exceed 17 tablespoons (246 mL) in any 8-week period (which is less than the amount of blood allowed to be drawn during that time frame under the American Association of Blood Banks standards) if you are receiving one dose vaccine or 24 tablespoons (354 mL) if you are receiving 2 vaccine doses.

The risks associated with having nasal swabs collected may include discomfort, eyes watering, bleeding, minor irritation and sneezing.

Data placed in the NIH-designated database will have identifiers removed, such as name, address, and identification numbers. Because it may be possible to re-identify genetic data, even if access to data is controlled, confidentiality cannot be guaranteed. There may be other risks that are unknown.

Risks and side effects you may experience with the study vaccines

After a study vaccination, a person might experience:

- **Mild to moderate events:**
    - A sore arm
    - Redness, swelling, hardness, or itching at injection site
    - Fever, chills, or fatigue (feeling tired)
    - Flu-like illness
    - Headache, muscle aches, pain and stiffness in the joints
    - Nausea or vomiting
    - Fainting
    - Swelling of lymph nodes in the neck or armpit
    - Decreased appetite
    - Lethargy (feeling sluggish or having little energy)
    - Night sweats
    - Malaise (a feeling of discomfort or feeling ill)
    - Diarrhea

Events such as a sore arm, fever, chills, fatigue, headache, muscle aches, pain and stiffness in joints, and nausea are more common after a second vaccination and may occur more commonly after additional booster vaccinations.

In a study of the Moderna mRNA-1273 booster vaccine, given as a single 50 mcg dose, headache, fatigue, muscle aches, joint aches, nausea or vomiting, chills, or a combination of those events, occurred in about three-quarters of people after vaccination. Fever occurred in about one in 10 people receiving the 50 mcg Moderna booster and pain at the injection site occurred in about eight in ten people.

In another study of the Moderna mRNA beta variant vaccine, given as a 50 mcg booster dose, fatigue, headache, muscle aches, joint aches, chills, nausea or vomiting, rash, or a combination of those events, occurred in six in ten people after vaccine. Pain at the injection site occurred in eight in 10 participants.

Similarly, in a study of the Pfizer BNT162b2 booster vaccine given as a single 30 mcg dose, reactions to the vaccine were mild to moderate and there were no serious side effects. Pain at the injection site occurred most often in 8 out of 10 participants, and other common reactions included:

- Fatigue (feeling tired)
- Headache
- Muscle/joint pain
- Chills

In a study of the Sanofi-GSK CoV2 preS dTM-AS03 vaccine given as 5 mcg booster dose to previously vaccinated participants, pain at the injection was reported in 8 out of 10 participants, which was more frequent in younger participants.

Other common reactions included:

- Headache
- Fatigue
- Muscle aches
- Joint aches
- Fever

Most reactions were mild.

About one in a one hundred people who received the Moderna mRNA-1273 primary series, given as two doses of 100 mcg vaccination, had a delayed reaction in the vaccinated arm, with redness and/or pain and/or itching starting about seven days after the vaccination. These events usually resolved over several days. There have also been reports of skin reactions, facial and lip swelling in people who have received cosmetic dermal fillers or implants.

In prior studies, swollen glands have been reported in less than 1% of participants receiving the Pfizer BNT162b2 vaccine and were also seen after the booster, but more frequently than with the first or second doses.

- **Severe events could occur very rarely:**
    - In prior studies with related study vaccines, less than 5% of participants receiving the Moderna mRNA-1273 vaccine and less than 1% of people receiving the Pfizer BNT162b2 vaccine had local pain and soreness around the vaccination site that

was considered "severe," meaning that it prevented them from performing their usual activities for some period of time.

- Rarely, an injection could cause an ulceration (open sore), abscess (a pocket of pus caused by the body fighting infection) or necrosis (dead tissue) at the injection site.
- An immediate allergic reaction called anaphylaxis (also known as allergic shock) may occur after receiving vaccines or medications.
- Anaphylaxis reactions have occurred after administration of the Moderna and Pfizer mRNA COVID-19 vaccines in vaccination campaigns under Emergency Use Authorization (EUA) in the United States. Most of these reactions started within 30 minutes of vaccination, most of those people had a prior history of allergy, and nearly all were women. The currently estimated risk of an anaphylactic reaction to the mRNA vaccines is about 2-5 events per million first vaccinations.

  This type of reaction may include symptoms such as:
  - Skin rash (hives)
  - Sweating
  - A feeling of dread
  - Swelling around the mouth, throat and eyes
  - Wheezing
  - Difficulty breathing
  - Increased pulse
  - Fainting or feeling dizzy due to low blood pressure
  - Inability to breathe without assistance

  If these reactions occur, emergency medications administered by study personnel can usually stop them. Most people who experience anaphylaxis recover completely. Rarely, people can die.
- Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have occurred in some people who have received the mRNA vaccines. In most of these people, symptoms began within a few days following receipt of the second dose of the vaccine. The chance of having this occur is very low. You should seek medical attention right away if you have any of the following symptoms after receiving the vaccine: chest pain, shortness of breath, or feelings of a fast-beating, pounding, or fluttering heart.
- One of the vaccines that you get in this study may contain a substance called AS03, which is an 'adjuvant'. This substance may improve the immune response to the vaccine. People who have received vaccines that contain an adjuvant, have very rarely (up to 1 in 10,000 people) developed illnesses called "autoimmune diseases", which can sometimes be serious and lifelong. Autoimmune diseases may develop when immune cells that normally protect you from illness, attack your own organs instead. These illnesses have also developed in people who have not received these vaccines.

- An increased risk of narcolepsy was observed in some individuals after vaccination with a flu vaccine containing AS03 (called Pandemrix) during the H1N1 pandemic in 2009-2010. Narcolepsy is an illness that affects your brain and causes uncontrollable sleepiness. People with narcolepsy sometimes go limp or fall asleep suddenly, such as while talking or driving, and it can be a lifelong problem. This study vaccine contains AS03. A similar risk of narcolepsy was not identified with other vaccines containing AS03. Currently available data suggest that the cases of narcolepsy seen immediately following the 2009-2010 pandemic in some people were most likely triggered by a reaction in those people to a protein from the flu virus itself that was also present in pandemic flu vaccines used at the time. Research is continuing to assess whether either of the main components of the 2009-2010 flu pandemic vaccine (e.g., the viral proteins in the form used in the vaccine or the AS03 adjuvant) may have contributed to the reaction.
- Additionally, any reaction other than the above events could be severe.

If you had an allergic reaction after being vaccinated in the past, or if you are allergic to any product, including polyethylene glycol (PEG), which is in the study vaccines, you must tell the study doctor or study staff before you decide to sign and date this informed consent form. If you have an allergy to some products, you will not be able to take part in this study. Serious allergic reactions can be life-threatening.

It is possible that receiving the study vaccines may change how your regular medications, vaccines, or supplements work. It is very important that you tell the study doctor about any medications, supplements, or vaccines before you take them during the study.

If you stop or change the dose of your regular medication, therapy, or supplements to be in the study, your health might get worse. Please tell the study doctor or study staff right away if you have any problems when you stop or change your regular medication, therapy, or supplements.

Please tell the study doctor or study staff right away if you have any side effects. Please tell them if you have any other problems with your health or the way you feel during the study, whether or not you think these problems are related to the study vaccine.

Ask the study doctor if you have questions about the signs or symptoms of any side effects that you read about in this consent form.

Risks Related to Pregnancy
You cannot be enrolled in this study if you are:

- Pregnant
- Nursing a child

COVID-19 vaccines appear to be safe in pregnancy, but there may be unknown risks to the embryo, fetus, or nursing child. Nobody knows what all of these risks are right now. If you can

become pregnant, you must have a negative urine pregnancy test before each study vaccination. You cannot participate in this study if you are breastfeeding.

If you become pregnant while you are in this study (through three months after the last vaccination), you should report this immediately to the study staff. With your permission, the study doctor or study staff will ask about your health, collect information from you through the outcome of your pregnancy, and collect scheduled blood samples. The study doctor may share this information with the study sponsor and with the Advarra Institutional Review Board (IRB), a group of people who review research studies to protect the rights and welfare of research participants.

BENEFITS
You may not benefit from being in this study. There may be benefit to getting a second booster of the original vaccine against SARS-CoV-2 if you are an adult 50 years or older, but we do not know whether vaccines based on the new variants will offer benefit.

However, the results of this research might benefit others by contributing knowledge that could lead to development of booster vaccine schedules for new strain variants of the SARS-CoV-2 virus.

ALTERNATIVES TO PARTICIPATION
The only alternative is to not participate in this study. You also may be able to receive a second booster outside of the study.

NEW FINDINGS
We will contact you about any new information and explain how this may affect your health, wellbeing, or willingness to stay in this study. You may be asked to sign and date a revised consent form if this occurs.

STUDY INFORMATION
When the results of this study are available, which will likely be a year or more after your last visit, we will attempt to provide you with a summary of those results, and a summary will be posted on http://www.ClinicalTrials.gov. If you move after your last study visit, it is your responsibility to provide us with your new address if you want to receive this information.

SOURCE OF FUNDING FOR THE STUDY
The study site is receiving payment from the NIH, National Institute of Allergy and Infectious Diseases (NIAID), Division of Microbiology and Infectious Diseases (DMID), the sponsor of the study.

Moderna, Pfizer and Sanofi-GSK, the companies that make the study vaccines, are providing the vaccines for this study to the NIH without charge.

COMPENSATION FOR PARTICIPATION

«Compensation»

You will be paid for your time and expenses related to participation in the study. You will receive $XX for each study visit where you are required to come to the clinic and $XX for a safety telephone call. Therefore, if you are in a group that received one dose of study vaccine you will receive $XXX and if you are in a group that received 2 doses of study vaccine you will receive $XXX. You will not be compensated for any missed visits. For illnesses you will be compensated $XX for each illness event where a swab is collected.

You will be paid _____ ***["following each completed visit", "monthly", "quarterly", "at the end of your participation in the research study", "following each completed visit or at the end of your participation in the research study, whichever you prefer"]***.

If you have any questions regarding your compensation for participation, please contact the study staff.

COST OF PARTICIPATION

While you are in the study, you still need to get regular medical care. You (and/or your health care payer) will still have to pay for the costs of your regular medical care that are not a part of this study. You will not have to pay to receive the study vaccine. There are no costs for the study visits, tests or procedures performed as part of this study.

To find out more about costs, ask the study staff.

COMPENSATION FOR INJURY

If you are injured as a result of being in this study, you should notify the study doctor as soon as possible. If there is an emergency, call 911 right away or go to the emergency room and contact your study doctor as soon as you can. If you tell the study staff that you think you have been injured then they will help you get the care you need.

If you are directly injured by the vaccine being studied, or by medical procedures needed because of this study, and you receive medical care for the injury, you may need to pay for that care. The study site will provide short-term medical care for any injury resulting from your participation in research here, but you might not be reimbursed for care covered and paid for by a third party like your health insurance provider, or costs such as required co-payments or deductibles related to that coverage. No long-term medical care or financial compensation for research related injury will be provided by the NIH or the Federal Government.

You do not give up any of your legal rights by signing and dating this form.

A Declaration under the Public Readiness and Emergency Preparedness (PREP) Act was issued by the Secretary of the United States Department of Health and Human Services on March 10, 2020. This Declaration limits the legal rights of a participant in clinical studies utilizing COVID-19

countermeasures, such as the study vaccines, mRNA-1273, used in this study. Because this study is covered by the PREP Act Declaration, covered persons, such as the manufacturers, study sponsor, researchers, healthcare providers and others have liability immunity (that is, they cannot be sued by you or your family under the laws of the United States).

If you believe that you may have been harmed as a result of this study, certain claims for serious injury or death caused by the countermeasure may be eligible for compensation through the Countermeasures Injury Compensation Program (CICP). This is a program set up by the Health Resources and Services Administration (HRSA) of the United States Government. Information about this program can be found at https://www.hrsa.gov/cicp/about/index.html or by calling 1-855-266-2427. If you are eligible for this program, you must file a claim within one year of the administration or use of the covered countermeasure. A factsheet on CICP and how to file a Request for Benefits Package to the CICP Summary, will be provided to you.

CONFIDENTIALITY

Paper documents containing personal information about you will be maintained in locked file cabinets. Computerized information will be maintained in password-restricted files. Only people who are involved in the conduct, oversight, or auditing of this study will be allowed access.

The authority to collect this information is provided by Title 42, Section 285f, of the US Code of Laws, which specifies that the general purpose of the National Institute of Allergy and Infectious Diseases is the conduct and support of research, training, health information dissemination, and other programs with respect to allergic and immunologic diseases and disorders and infectious diseases, including tropical diseases.

By signing and dating this consent form you are giving permission for representatives of the NIH, the Office for Human Research Protections (OHRP), the FDA, and Advarra IRB (a group of people who review research studies to protect the rights and welfare of research participants), as well as the study doctor and other employees of the study site involved with this research study, to inspect sections of your medical and research records related to this study.

The FDA may choose to inspect your records since you are a participant in this research study. When a study is submitted to the FDA, the study doctor agrees to allow the FDA access to the study records. The FDA will treat the information as confidential, but on rare occasions disclosure to third parties may be required by law. Therefore, absolute protection of confidentiality cannot be promised.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CERTIFICATE OF CONFIDENTIALITY

To help us protect your privacy, we have a Certificate of Confidentiality from the NIH. Study staff cannot provide to any person not connected with the research your name, or any materials that contain identifiable, sensitive information about you, unless permitted by a legal exception, such as state laws that require reporting of some contagious diseases. The most important protection provided by the Certificate is that the study staff cannot be forced to provide any of your identifiable, sensitive information, in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, such as if there is a court subpoena, without your permission.

The study team will use the Certificate to resist any demands for information that would identify you.

Your information protected by the Certificate may still be disclosed or used when the information:

1. Is disclosed to people connected with the research; for example, information may be used for auditing or program evaluation internally by the NIH; or
2. Is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the FDA. This does not include disclosure for use during legal proceedings as noted above;
3. Is necessary for your medical treatment and you have consented to this disclosure;
4. Is for other scientific research as allowed by applicable federal regulations;
5. Is disclosed with your consent.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing and dating below you consent to those disclosures.

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

If you decide to be in this study, the study doctor and study staff will use and share health data about you to conduct the study. Health data may include your name, address, phone number, date of birth, medical history and information about your study visits including all tests.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study staff may share health data about you with authorized users including:

- The Department of Health and Human Services
- The OHRP
- Additional governmental agencies in the United States
- Advarra IRB
- Your regular doctor
- The Food and Drug Administration (FDA) and other US federal and state agencies.
- A public health authority that is authorized by law to collect or receive such information for the purpose of preventing or controlling disease, injury, or disability, and conducting public health surveillance, investigations, or interventions.
- Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and sponsor and need to access your information to conduct this study.
- Other research doctors and medical centers participating in this study

Your health data will be used to conduct and oversee the research, including for instance:

- To do the research
- To study the results
- To see if the research was done correctly

If the results of this study are made public information that identifies you will not be used.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will last indefinitely. In California and any other state that requires an expiration date, the Authorization will expire 50 years after you sign and date this authorization document.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered

after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

STATEMENT OF AUTHORIZATION

I have read this form and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

- Whom to contact in the case of a research-related injury or illness;
- Payment or compensation for being in the study, if any;
- Your responsibilities as a research participant;
- Eligibility to participate in the study;
- The study doctor's or study site's decision to exclude you from participation;
- Results of tests and/or procedures;

Please contact the study doctor at the telephone number listed on the first page of this consent document.

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

- By **mail**:
  Study Subject Adviser
  Advarra IRB
  6100 Merriweather Dr., Suite 600
  Columbia, MD 21044
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00062043.

VOLUNTARY PARTICIPATION / WITHDRAWAL

Your signature and date on this consent form means that you have received the information about this study and that you agree to be a part of the study. Your participation in this study is voluntary. You may decide not to participate, or you may discontinue participation at any time without penalty if you agree to participate and then decide that you no longer want to be in the study. Your decision will not result in any penalty or loss of benefits to which you are entitled.

You will be given a copy of this signed and dated consent form to keep. You are not giving up any of your rights by signing and dating this consent form. Even after you have signed and dated this consent form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

The study doctor or sponsor may decide to stop you from taking part in this study at any time, without your consent. You could be removed from the study for any of the following reasons:

- You miss research visits
- You are unable to comply with study procedures or instructions
- You withhold information about your health history or medications
- Reasons related to your health
- If you have a serious reaction to the study vaccine
- Because the entire study is stopped (the sponsor may stop the study at any time)
- If you do not later consent to any future changes that may be made to the study
- If you become pregnant
- Any other reason

If you decide to stop or the study doctor withdraws you, we may ask you to come for a final visit. This visit may include activities listed in the general study visits. We will stop collecting your information and specimens for research when you withdraw your consent for the research or are withdrawn by the study doctor. However, any information and specimens collected prior to withdrawal may continue to be used for this study.

Advarra Institutional Review Board (IRB), the FDA, other regulatory agencies, or the sponsor (NIH) who oversee the conduct of this study can stop the study at any time for safety concerns or other issues.

CONSENT

I have read (or have had read to me) and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I agree to participate in this study. I will receive a copy of this signed and dated consent document.

_____

Printed Name of Participant

_____ _____

Signature of Participant Date

I attest that the participant named above had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to be in this study.

_____

Printed Name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent Date