Duke University Health System

Consent to Participate in a Research Study
ADULT
A Phase 1 Open-Label, Comparator-Controlled, Dose-Escalation Study to Evaluate the Safety and Immunogenicity of a Single Dose of VRC H1ssF_3928 mRNA-LNP in Healthy Adults
DMID 21-0010
Version 8.0 06JUN2024

CONCISE SUMMARY

This is a research study to understand what happens when a person receives one of three dose levels of an investigational messenger ribonucleic acid (mRNA) influenza vaccine and how the body responds to the dose received. Participation in this research is voluntary. To do this research, 10 participants will be enrolled into each group to receive either a low dose (10 microgram [mcg]), medium dose (25 mcg), or high dose (50 mcg) of the investigational vaccine. Dosing will start at the 10 mcg dose level and only increase to the next level if no concerning side effects are found. Once determined which dose level is most tolerable and safe, a group of 10 additional participants will receive that particular dose to be studied further. To compare, a separate group of 10 participants will receive one of the US Food and Drug Administration (FDA) approved seasonal flu vaccines (IIV4). All study vaccine will be administered in the upper arm. We will draw blood (varying from 2 tablespoons to about 7-½ tablespoons per visit) from the arm to monitor the safety of the vaccine and to measure the levels of antibody against the flu virus in the body that are present both before and after receiving the vaccine. We will also obtain samples from the nose using a filter paper to test for levels of antibody against the flu virus. If a flu-like illness occurs we will collect a nasal swab to test for the presence of the flu virus.

Blood and nasal samples will be stored for future research to further the understanding of influenza infection. Providing these samples is required for participation in this study. Genetic testing may be performed on blood samples collected during this study after the study is over. The results of these tests will not be shared. If you do not want to provide these samples, you should not agree to participate in this study.

Participation in this study will last approximately 12 months with a screening visit to determine eligibility, one vaccination visit and eight follow up research clinic visits.

The risks involved in participating in this study are described in detail below. Some of the more common risks to receiving an influenza vaccine include symptoms of flu-like illness such as fever, tiredness, body aches, chills, headaches, nausea, and vomiting along with redness, swelling and bruising at the injection site. Risks associated with mRNA vaccines for COVID-19 made in a similar way to this investigational vaccine include myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart). These events are rare and have occurred particularly in adolescents and young adult males after the second dose of COVID-19 mRNA vaccine. Risks associated with blood draws include discomfort, bruising and fainting. Nasal absorption samples or nasal swabs can cause mild discomfort and bleeding in the nose and watery eyes.

If you are interested in learning more about this study, please continue reading below.

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This research study involves the testing of a first-in-person investigational influenza virus (flu) vaccine or flu shot. "Investigational" means that the vaccine has not been approved for use outside of research studies, or licensed for sale in the United States by the Food and Drug Administration (FDA), the government agency that licenses new vaccines. You are being asked to take part in this study because you are between 18 and 49 years of age, you are in good overall health, able to comply with the study procedures, and able to provide consent for your participation.

Research studies are voluntary and include only individuals who choose to take part. Before you decide to participate, it is important for you to know why the research is being done, what it will involve and what the possible risks are. Therefore, it is important you read and understand the following explanation of the study. Ask us if there is anything that is not clear or if you would like more information. Please take your time to make your decision. You may wish to discuss the study with family, friends, and/or your own doctor. Feel free to ask any questions before you agree to take part in the study. Also, please tell the study doctor or study staff if you are taking part in another research study.

Emmanuel Walter, MD, MPH will conduct the study and it is funded by the National Institute of Allergy and Infectious Diseases (NIAID), which is part of the National Institutes of Health (NIH). The sponsor of this study, NIAID, will pay Duke University to perform this research, and these funds may reimburse part of Dr. Walter's salary.

WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate, Dr. Emmanuel "Chip" Walter will be your doctor for the study and will be in contact with your regular health care provider throughout the time that you are in the study and afterwards, if needed.

WHY IS THIS STUDY BEING DONE?

Vaccines help your body produce both antibodies and immune cells in the blood to help you develop protection from a disease. This study is being done to explore the level of protection to the flu that results following receipt of an investigational vaccine. This investigational vaccine is named VRC H1ssF_3928 mRNA-LNP. The study will also be used to collect information (such as side effects) following receipt of the vaccine and to plan for potential future studies.

The flu is caused by influenza viruses and is very contagious. In most people the flu causes a relatively mild or moderate illness with fever and cough, but sometimes the flu can be more severe, resulting in pneumonia and, in rare cases, death. In the United States, an annual seasonal flu shot is recommended for all persons over six months of age to help protect against the flu. The current seasonal flu shot protects against four different strains of flu but is only partly effective, and it must be given on a yearly basis, as protection decreases over the course of a flu season. There is a need to develop improved flu

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vaccines that are more effective, last longer, and can help protect against new flu strains that may circulate. To address this unmet need, we are evaluating the side effects and protection following receipt of the investigational VRC H1ssF_3928 mRNA-LNP vaccine. VRC H1ssF_3928 mRNA-LNP vaccine is given by injection using a needle. This study will test the vaccine at three different dose levels (amounts of vaccine). Some people in this study will also get the traditional flu shot. You and the study team will know which vaccine you receive, and if you receive the VRC H1ssF_3928 mRNA-LNP vaccine, you will know the dose you receive.

VRC H1ssF_3928 mRNA-LNP vaccine is made in a similar manner to the current mRNA COVID-19 vaccines that FDA has approved for use. The VRC H1ssF_3928 mRNA-LNP vaccine does not contain the whole flu virus or the parts of the flu virus that can make you ill. Instead, the vaccine is made up of part of the flu virus' genetic code from one flu strain in addition to the genetic code from an iron-carrying protein named ferritin from the bacteria *Helicobacter pylori (H. pylori)*. The genetic material is surrounded by fatty particles called lipids to help keep the genetic material from degrading. They use a person's cells' protein-making machinery to produce the ferritin protein and a part of the hemagglutinin protein named "stem protein" seen on the outside of the flu virus, which is common to many flu strains. This stem and ferritin protein, made by your body, combine together in one particle and may help your body produce antibodies to fight against the flu. We will check how many antibodies and immune cells your body makes by taking blood samples and testing them.

We will compare the side effects that participants experience following receipt of the VRC H1ssF_3928 mRNA-LNP vaccine against people receiving different dose levels of the vaccine. We will also compare the levels of antibody and immune cells in the blood between people receiving different dose levels of VRC H1ssF_3928 mRNA-LNP and people receiving the traditional flu shot.

The three different doses of the VRC H1ssF_3928 mRNA-LNP vaccine being tested include: a low dose of 10 micrograms (mcg), a medium dose of 25 mcg, and a higher dose of 50 mcg. Dosing will start at the lowest dose (10 mcg) and only increase to the next highest dose if it is determined that there are no concerning side effects. Up to 10 participants will receive each dose level. A determination of the highest dose level with the most acceptable side effect profile and an additional 10 participants will receive that dose. Ten separate participants will be enrolled to receive the standard seasonal flu shot (Fluzone Quadrivalent, manufactured by Sanofi Pasteur, Inc.). All study injections will be given into the muscle of the upper arm.

Blood samples will be collected to measure levels of antibodies and immune cells in the blood before and after the injections, and the safety and tolerability of the vaccine will be evaluated. We will also collect samples from the nose using a filter paper to measure the levels of antibodies in the nose. The results of these tests will not be shared with you.

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HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Up to 120 people may be consented for this study at Duke, and we hope to have 50 participants to evaluate.

WHO SHOULD TAKE PART IN THIS STUDY?

To be in this study, you should be 18 to 49 years of age and in general good health. If you take part in this study, you must not have health conditions that weaken your body's ability to fight infections or be taking drugs that weaken the body's ability to fight infections, or have infection with human immunodeficiency virus (HIV), hepatitis B virus, or hepatitis C virus. If you take part in this study, you must refrain from receiving another investigational agent or participate in another clinical trial with an investigational agent within 60 days before study vaccination through the entire study period of about 12 months. You must not receive any other approved or authorized vaccines within 60 days before or after the study vaccination. You must refrain from receiving the flu vaccine within 90 days before and 60 days after the study vaccination. You must also refrain from blood donation within 30 days before and 60 days after the study vaccination.

If you are a person able to have children, the study doctor or study staff will perform a pregnancy test via blood draw at the first study visit (screening visit) and urine pregnancy test before the study vaccination visit. If a pregnancy test is positive, you may not participate further in the study. You must not be breastfeeding or plan to breastfeed or become pregnant 30 days prior to receiving the study vaccine or 30 days after receiving study vaccine. If you are 40 years old or older, there is a chance of a false positive or indeterminate blood pregnancy test and additional testing may be required. You must have been using an acceptable method of birth control (for example, an intrauterine device or hormonal methods) for at least 30 days prior to receiving study vaccine and agree to continue using an acceptable method of birth control until at least 30 days following receipt of study vaccine.

If you are a person able to father children, receiving VRC H1ssF_3928 mRNA-LNP, and sexually active with a person able to have children, you must agree to either refrain from having any type of sexual intercourse, or use a male condom for all types of intercourse for 60 days after receiving the study vaccine. You must also refrain from donating sperm for 60 days after receiving the study vaccine.

There may be other reasons why you cannot participate in this study. The study doctor or study staff will discuss these with you.

WHAT IS INVOLVED IN THE STUDY?

If you agree to be in this study, you will have 10 scheduled in-person study visits and possibly more if an unscheduled visit is needed. Every visit will include a blood draw and six visits will include a nasal absorption specimen. The total amount of blood drawn throughout the entire study period of one year is

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approximately 809 mL (55 tablespoons). Approximately 271 mL (18 tablespoons) of the blood drawn will be collected for storage and used for future, yet unknown, testing that is not part of this study. The amount of blood drawn at each visit will vary between 29 mL (2 tablespoons) to 109 mL (7-½ tablespoons). Each study visit is detailed below.

Visit 0 - Screening Visit
The first visit will be a screening visit to help determine if you are eligible to participate. At this visit, you will be asked to sign and date this consent form. No study activities will occur until you decide that you want to participate and sign/date the form.

Eligible participants will also be asked to sign a separate consent form for the biorepository protocol (Pro00104290, DMID Protocol No. 19-0025), for the storage and use of leftover and extra samples and associated data for the purpose of future research on influenza. Your samples and data will be coded (no information that can be used to identify you will be connected to your samples or data). In addition to the nasal samples, some of the blood being collected at each study visit below will not be used for studies as part of this study, but will be collected and stored in the biorepository for use in future research. More information regarding the repository protocol is below in the section regarding future use.

Once you sign/date this consent form, the following screening procedures will be done to see if you are eligible for the study.

- Review eligibility criteria
- We will collect demographic data such as sex, age, ethnicity, and race
- We will review and document your medical history and recent medications taken within the last 90 days
- We will collect a history of any medication allergies including a hypersensitivity to any components of the study products
- We will ask if you are participating in another clinical trial or plan to enroll in another clinical trial during the study period
- We will document your influenza vaccinations for the 2021-2022, 2022-2023, and 2023-2024 influenza seasons
- We will obtain vital signs: oral temperature, heart rate, blood pressure
- We will measure your height and weight
- You will have a physical exam
- We will collect approximately 30 mL (about 2 tablespoons) of blood from a vein in your arm for laboratory tests, including blood counts, blood chemistry tests and troponin level. Although troponin level is not a standard test after the screening visit, the study doctor or licensed clinician

may test for troponin during follow up visits if it is clinically indicated. This will also include tests to see if you are infected with hepatitis B, hepatitis C, or HIV, the virus that causes AIDS.

- You will be notified of the results of the testing, and counseled as to the meaning of the results, whether they are positive or negative. We are required to report all positive hepatitis B, hepatitis C and HIV results to the North Carolina Division of Public Health. The test results will be kept confidential to the extent permissible under the law. As part of this protocol, you will be tested for hepatitis B and C, which causes liver damage and liver failure. If the test indicates that you are infected with hepatitis B or C or HIV, you will receive additional counseling about the significance of your care and possible risks to other people.
- If you do not want to be tested for hepatitis B and C or HIV, then you should not agree to participate in this study. The study doctor or study staff will provide pre-test counseling for the HIV/AIDS tests so you will have information about the risks and benefits of being tested.
- In rare cases, an HIV test result may be 'indeterminate', which means that it is not possible to say if it is positive or negative. This can occur for several reasons and most people with indeterminate tests do not have HIV. Indeterminate tests are not notifiable conditions and this information is not reported to the local health department.
- If the hepatitis B or C or HIV tests are positive or if other tests are outside an acceptable range, you will not be able to continue in the study. Abnormal results will be provided to you for follow-up with your provider.

- You will have a urine drug screen to test for non-prescribed amphetamines, cocaine, and opiates.
- If you are a person who is able to become pregnant you will have a blood pregnancy test at this visit and will be counseled to practice true abstinence or use at least one primary form of contraception from 30 days prior to receipt of the study vaccine until 30 days after receipt of the study vaccine.
- If you are a person who could potentially father children, you will be counseled to refrain from sperm donation and abstain from sexual intercourse or use male condoms from the date of receipt of the study vaccine until 60 days after receipt of the study vaccine. (This does not apply to men in the group receiving the quadrivalent seasonal influenza vaccine, IIV4.)
- You will have an electrocardiogram (ECG; heart tracing) performed to see if you are healthy enough to participate in the study.
  - An ECG is a test that records the electrical activity of the heart. Small self-adhesive patches called electrodes are placed on select locations of the skin on the arms, legs, and chest. The test usually takes less than a minute to perform once the patches are in place. The ECG machine creates a paper print out of the electrical activity of the heart for the doctor to review.

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The screening visit may take up to 2 hours. If the evaluations obtained at the screening visit confirm that you are eligible, the vaccination visit will be scheduled within 2 weeks of the screening visit.

Visit 1 - Vaccination Visit

This visit will take approximately 2 hours and will consist of:

- Review and confirm eligibility
- We will review your medical history and update if needed
- We will review your current medications and influenza vaccination history
- We will obtain vital signs: oral temperature, heart rate, blood pressure
- A physical exam will only be obtained if the study investigator thinks it is necessary
- Approximately 109 mL (7-½ tablespoons) of blood will be collected from your arm to test for blood counts, blood chemistry, troponin level and immune testing to determine your body's baseline level of protection from the flu. Some of the blood will be used for future, yet unknown, testing.
- At this visit, persons able to get pregnant will have a urine pregnancy test. Those with a positive test will not be able to continue in this study. You will also be counseled to continue the method of birth control discussed at the screening visit.
- If you are a sexually active man, you will be counseled to refrain from sperm donation and abstain from sexual intercourse or use condoms from the date of receipt of the study vaccine until 60 days after receipt of the study vaccine. (This does not apply to men in the group receiving the quadrivalent seasonal influenza vaccine, IIV4.)
- We will obtain a nasal absorption sample by placing a small synthetic filter paper material into one side of your nasal passage.
- Depending on what dose level the study is evaluating at time of vaccination visit, you will receive either the low dose (10 mcg), medium dose (25 mcg), high dose (50 mcg) or a standard seasonal influenza shot (IIV4) into the muscle of your upper arm. You will need to stay at the study clinic for at least 30 minutes after your injection to be watched for study injection reactions. Study staff will look at your arm and the site of the shot before you leave.
- A study staff member will give you a paper memory aid or send you an electronic memory aid, ruler and thermometer, and will show you how to use them for the study. You will be asked to write down your temperature and any symptoms that you experience every day, starting the evening of the study vaccination, and continuing for the next 13 days. You should also write down any drugs or medicines you take during this time, even over-the-counter medicines such as Tylenol®. You should contact the study staff if you have any severe reactions in the week after the study injection. These reactions are described later in this form.

Follow up visits will take approximately 30 minutes and will consist of:

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Clinic Visit 2 (Day 3 +/- 1 days)

- Approximately 29 mL (2 tablespoons) of blood will be taken from your arm for safety and immune tests to determine the level of protection in your body from the flu and for future research use on influenza.

Study staff will obtain:

- vital signs and a nasal absorption sample.
- An ECG will be performed.
- We will review your influenza vaccination history, medications and the Memory Aid diary with you.
- A physical exam may be performed.
- Persons able to become pregnant or father children will receive abstinence and contraception counseling.

Clinic Visit 3 (Day 8 +/- 2 days)

- Approximately 105 mL (7 tablespoons) of blood will be taken from your arm for safety and immune tests to determine the level of protection in your body from the flu and for future use.
- Study staff will obtain vital signs and a nasal absorption sample.
- A physical exam and/or ECG may be performed.
- We will review your influenza vaccination history, medications, and the Memory Aid diary with you.
- Persons able to become pregnant or father children will receive abstinence and contraception counseling.

Clinic Visit 4 (Day 15 +/- 2 days)

- Approximately 84 mL (5-½ tablespoons) of blood will be taken from your arm for immune testing to determine the level of protection in your body from the flu and for future use.
- Study staff will obtain vital signs and a nasal absorption sample.
- A physical exam and/or ECG may be performed.
- We will review your influenza vaccination history, medications, and the Memory Aid diary with you.
- Persons able to become pregnant or father children will receive abstinence and contraception counseling.

Clinic Visit 5 (Day 29 +/- 3 days)

- Approximately 100 mL (7 tablespoons) of blood will be taken from your arm for safety and immune testing to determine the level of protection in your body from the flu and for future use.

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- Study staff will obtain vital signs and a nasal absorption sample.
- We will review your influenza vaccination history and medications with you, any new or worsening medical problems.
- A physical exam and/or ECG may be performed.
- Persons able to become pregnant or father children will receive abstinence and contraception counseling.

Clinic Visit 6 (Day 57 +/- 3 days)

- Approximately 100 mL (7 tablespoons) of blood will be taken from your arm for safety and immune testing to determine the level of protection in your body from the flu and for future use.
- Study staff will obtain a nasal absorption sample.
- Vital signs may be obtained.
- We will review your influenza vaccination history and medications with you, any new or worsening medical problems.
- A physical exam and/or ECG may be performed.
- Persons able to become pregnant or father children will receive abstinence and contraception counseling.

Clinic Visit 7 (Day 85 +/- 7 days)

- Approximately 84 mL (5-½ tablespoons) of blood will be taken from your arm for immune testing to determine the level of protection in your body from the flu and for future use.
- Vital signs may be obtained.
- We will review your influenza vaccination history and medications with you, any new or worsening medical problems.
- A physical exam and/or ECG may be performed.

Clinic Visit 8 (Day 181 +/- 7 days)

- Approximately 84 mL (5-½ tablespoons) of blood will be taken from your arm for immune testing to determine the level of protection in your body from the flu and for future use.
- Vital signs may be obtained.
- We will review your influenza vaccination history and medications with you, any new or worsening medical problems
- A physical exam and/or ECG may be performed.

Clinic Visit 9 (Day 366 +/- 7 days)

- Approximately 84 mL (5-½ tablespoons) of blood will be taken from your arm for immune testing to determine the level of protection in your body from the flu and for future use.

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- Vital signs may be obtained.
- We will review your influenza vaccination history and medications with you, any new or worsening medical problems.
- A physical exam and/or ECG may be performed.

Unscheduled Visit
You may be asked to come back to the study clinic at other times if needed to review your health. This visit may be conducted by phone or telehealth if an in-person visit is not possible. Study personnel will determine what activities will be needed after reviewing any symptoms that you are having. This visit may consist of:

- Obtaining blood for safety and immune testing
- Collecting vital signs: oral temperature, heart rate and blood pressure
- A physical exam
- Collecting a nasal absorption sample, if needed
- Collecting a nasopharyngeal swab to test for influenza virus. A cotton-tipped swab will be gently passed through your nostril to the back of your nose
- An ECG
- Reviewing medications and influenza vaccination history
- Review of new or worsening medical conditions

Influenza-like Illness Visits
During the study, participants will be requested to report if they have any influenza-like illness (ILI) starting from the day of screening through Day 366. Participants reporting influenza or ILI will be evaluated. ILI is defined as fever (temperature of 100°F [37.8°C] or greater) and a cough and/or sore throat in the absence of a known cause other than influenza. If you have an ILI, a nasopharyngeal swab will be collected to test for the presence of the influenza virus.

Early Withdrawal Visit
If you stop taking part in this study for any reason, you may be asked to return to the study center for a final visit. You will be asked about any reactions, illnesses, or any new or worsening medical problems you may have had since your last clinic visit. You also may be asked about any medications you may have taken or if you received an influenza vaccine since your last study clinic visit. A brief physical examination may be done and blood samples may be taken along with vital signs, nasal absorption and an ECG may be performed. Persons able to become pregnant or father children may receive abstinence and contraception counseling.

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BLOOD AND NASAL SAMPLE STORAGE FOR FUTURE USE

As part of this study, we are obtaining blood and nasal samples from you for this study and extra samples for a repository (a place that stores samples). At the time of screening, eligible participants will be required to sign a separate consent form for the separate biorepository protocol, for the storage and use of both extra nasal and blood samples as well as leftover samples and associated data (information) in future research. This will not include protected health information, such as your name and date of birth. If you do not want your leftover samples to be used for future research, you should not agree to participate in this study.

Secondary research is research that is not part of this flu study but will be performed in the future. You will not be told about the secondary research or any results. Types of research include new or different immunological laboratory tests to provide information for the development of new flu vaccines, or to better understand flu virus or other infections. New genetic testing, including DNA testing, may occur. The tests we might want to use to study your blood and nasal samples may not even exist at this time. The consent form for the repository protocol will explain the types of genetic testing, how the data will be stored in databases, how this information will be shared with other researchers, and whether information will be shared with you.

After enrollment, you may withdraw your consent for the collection and storage of samples for secondary research at any time by providing written notice to the investigator or study staff. No "extra samples" will be collected. Samples collected for this vaccine study may not be destroyed. However, samples collected or stored for secondary research may be destroyed after the vaccine study is completed. Samples released for secondary research before you withdrew consent may not be able to be destroyed.

The samples will not be sold or used directly for production of any commercial product. However, the research studies in the future could indirectly lead to a commercial product that protects against flu 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.

HOW LONG WILL I BE IN THIS STUDY?

Your participation in this study will last up to approximately 366 days (12 months), not including the screening period that will take place up to 14 days prior to Visit 1.

You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled. However, if you decide to stop participating in the study, we encourage you to talk to your doctor first. Any clinically relevant results will be shared with you.

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WHAT ARE THE RISKS OF THE STUDY?
While on the study, you are at risk for some side effects. You should discuss these with the study doctor or study staff. Many side effects go away shortly after a vaccine is given, but in some cases, side effects can be serious, long lasting, or permanent.

Study risk is minimized by slowly increasing the dose being tested and by first testing each dose of vaccine in just two participants and pausing before enrolling the remaining participants receiving that dose.

This investigational influenza vaccine, VRC H1ssF_3928-mRNA-LNP, has never been tested in humans. There may be risks that we do not know about, which include your health getting worse or even death. Side effects that have been reported with similar mRNA vaccine include at the injection site:

- Pain
- Tenderness
- Swelling (hardness)
- Redness
- Swelling of the lymph nodes on the same arm of the injection
- Difficulty moving your arm

General side effects include:

- Fatigue
- Headache
- Muscle pain
- Joint pain
- Chills
- Nausea
- Vomiting
- Fever
- Feeling unwell
- Fainting
- Abnormal dreams
- Low white blood cells

There is a small possibility that an mRNA vaccine could cause a severe allergic reaction occurring shortly after getting a dose of vaccine. Participants with a prior history of severe allergic reaction after a previous dose of any influenza vaccine or mRNA vaccine or to a vaccine component will not be allowed to receive vaccine.

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Signs of severe allergic reaction can include:

- Difficulty breathing
- Facial and throat swelling
- Rapid or irregular heartbeat
- Body rash
- Dizziness
- Weakness

Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have occurred in some people who have received mRNA-LNP COVID-19 vaccines (Pfizer-BioNTech and Moderna). These events have occurred particularly in adolescents and young adults after the second dose.

In a population-based cohort study the incidence of acute myocarditis was noted to be almost 6 per 1 million individuals after the second dose. Myocarditis reporting rates among males 12-29 years of age have been noted to be about 40 cases per million second doses of mRNA COVID-19 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 low. Symptoms include:

- Chest pain
- Shortness of breath
- Palpitations (fast beating or fluttering heart)

Because this vaccine encodes for the iron carrying ferritin protein from the *H. pylori* bacteria, it is theoretically possible that your body could respond by making antibodies against human ferritin. Cross-reactive anti-ferritin antibodies have not been observed in animals receiving *H. pylori* ferritin. Study participants will be closely monitored via blood draws for levels of iron, ferritin, and anti-ferritin antibodies.

In laboratory animals, abnormalities associated with increased clotting were seen following administration of the H1ssF_3928 protein. Study participants will be closely monitored via blood draws for changes in prothrombin time (PT), activated partial thromboplastin time (APPT), and fibrinogen levels. These are ways to measure how your blood is clotting.

Available data from short-term follow-up suggest that most individuals have had resolution of symptoms, but information is not yet available about potential long-term effects. In addition, there may be other possible unknown side effects of mRNA-LNP vaccines. Serious and unexpected side effects may also occur. Should a severe allergic reaction occur immediately following vaccination, medications

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to treat such a reaction will be immediately available for administration according to standard guidelines at the study site.

Seasonal Influenza Vaccine/Shot (IIV4) Risks
IIV4 risks include minor problems such as:

- Soreness, redness, swelling, or pain where the shot was given
- Hoarseness of the voice
- Sore, red or itchy eyes
- Cough
- Fever
- Body aches
- Headache
- Itching
- Fatigue

All of these side effects usually occur within 1-2 days of vaccination and usually resolves without treatment. More serious problems including a small increased risk of Guillain-Barré Syndrome estimated at 1 or 2 additional cases per million people vaccinated can occur. Guillain-Barré Syndrome is a disorder of the immune system where the nerves are attacked by immune cells that causes weakness and tingling in arms and legs. In addition, IIV4 rarely can cause a severe allergic reaction, or anaphylaxis, which is estimated at ~1 in one million doses of IIV4 administered.

Participants with a prior history of severe allergic reaction after a previous dose of any influenza vaccine or to a vaccine component, including egg protein, and participants with a history of Guillain-Barré Syndrome will be excluded from study enrollment.

Should a severe allergic reaction occur immediately following vaccination, medications to treat such a reaction will be immediately available for administration according to standard guidelines at the study site.

Risks related to Nasal Absorption or Nasal Swab Sampling
Obtaining a nasal absorption or nasal swab sample can cause discomfort in the nostrils, a nosebleed, tickling in the throat, coughing, sneezing, or watery eyes at the time of collection.
Risks of electrocardiogram (ECG)
The electrodes of an ECG may feel cold when applied; in rare cases, a rash, itching, redness or skin irritation develops where the patches are placed. This type of irritation usually resolves by itself, but topical medication is occasionally required.

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Risks related to blood draws
Having blood taken from your arm can cause temporary pain and discomfort, bruising, and fainting with a rare risk of clotting, excess bleeding, and infection. In addition, anemia may be a risk with the blood collection.

If I Catch Influenza, Could the Antibodies Produced Following Vaccination Make It Worse?
For other vaccines tested in animals against similar viruses (but not influenza), there have been reports of the illness being more severe in the animals that received the product than in those animals that did not. So far, this has not been seen with influenza. It remains important for you to contact your study doctor if you develop symptoms that might be caused by influenza (for example, fever, cough, shortness of breath).

Reproductive Risks
Pregnancy can affect the body's response to vaccines. In addition, the effects of VFC H1ssF_3928 mRNA-LNP on a pregnant person, developing pregnancy, or breastfeeding infant are not known, and it may be present in semen and transmitted to a partner during sexual activity. For these reasons, people who are pregnant, planning to become pregnant or father a child, or breastfeeding are not allowed to participate in this study. Pregnancy testing and contraception requirements for people able to become pregnant or father a child are described in detail above.

If you or your partner should become pregnant while you are in this study, you should report this immediately to the study staff. With your permission and additional consent from the pregnant woman, the study doctor or study staff will ask about your health and the outcome of the pregnancy. The study doctor may share this information with the sponsor and the Institutional Review Board (IRB), a group of people who review research studies to protect the rights and welfare of research participants. If additional consent is not provided by your pregnant partner, the pregnancy outcome and date of delivery may be requested from the research participant.

There may be risks, discomforts, drug interactions or side effects that are not yet known.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
If you agree to take part in this study, no direct medical benefit is expected. As this is a first-in-person trial, it is unknown whether the study product, VRC H1ssF_3928 mRNA-LNP, will help to protect participants from influenza disease or, if it does, how long that protection may last. The immunogenicity comparator IIV4 (seasonal flu vaccine/shot) may offer some protection against influenza infection for the strains of influenza contained in the vaccine.

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We hope that in the future the information learned from this study will benefit other people.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?
Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total confidentiality. Your personal information may be viewed by individuals involved in this research and may be seen by people including those collaborating, funding, and regulating the study. We will share only the minimum necessary information in order to conduct the research. Your personal information may also be given out if required by law.

As part of the study, results of your study-related laboratory tests and procedures may be reported to NIAID and its affiliates. In addition, your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the FDA, representatives and affiliates of NIAID, the Duke University Health System (DUHS) IRB, and others as appropriate. If any of these groups review your research record, they may also need to review your entire medical record.

As part of this study, you will be asked to have certain tests and/or procedures performed. These test results will be recorded in your medical record and will be reported to representatives and affiliates of NIAID. Results of tests and studies done solely for this research study and not as part of your regular care will not be included in your medical record.

The Department of Health and Human Services (HHS) has issued a Certificate of Confidentiality to further protect your privacy. With this Certificate, the investigators may not disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings, unless you have consented for this use. Research information protected by this Certificate cannot be disclosed to anyone else who is not connected with the research unless:

1) there is a law that requires disclosure (such as to report child abuse or communicable diseases but not for legal proceedings);
2) you have consented to the disclosure, including for your medical treatment; or
3) the research information is used for other scientific research, as allowed by federal regulations protecting research participants.

Disclosure is required, however, for audit or program evaluation requested by the agency that is funding this project or for information that is required by the FDA.

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If you

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want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

All of the blood, urine and procedures are being done only because you are in this study. The study results for labs processed locally such as HIV and hepatitis B, will be available in your medical record. Laboratory results that are sent out of DUHS, will not be a part of your research or medical record.

The study results will be retained in your research record for at least six years after the study is completed or for two years after study product licensure, whichever is longer. At that time either the research information not already in your medical record may be destroyed or information identifying you will be removed from such study results at DUHS. Any research information in your medical record will be kept indefinitely.

This information may be further disclosed by the sponsor of this study. If disclosed by the sponsor, the information is no longer covered by federal privacy regulations.

If this information is disclosed to outside reviewers for audit purposes, it may be further disclosed by them and may not be covered by federal privacy regulations.

While the information and data resulting from this study may be presented at scientific meetings or published in a scientific journal, your name or other personal information will not be revealed.

A description of this clinical trial will be available on https://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.

We will keep your participation in this research study confidential to the extent permitted by law. However, it is possible that other people, such as those indicated below, may become aware of your participation in this study and may inspect and copy records pertaining to this research. Some of these records could contain information that personally identifies you. Reviewers may include:

- Federal government regulatory agencies
- The FDA
- The NIH and those contracted by the NIH, such as Emmes Company, Inc and Technical Resources International (TRI) pharmacovigilance and study monitoring groups
- Auditing departments of Duke University
- The DUHS IRB (a committee that reviews and approves research studies) and other representatives of this organization

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To help protect your confidentiality, we will use ID numbers on research data. The data will be stored in locked cabinets and/or offices when not in use. Only research team members who are involved in the conduct, oversight, or auditing of this study will have access to the research data.

Electronic data will be stored in password protected computers and websites. For this study, each blood and nasal sample will be labeled with a barcode and a unique tracking number to protect your confidentiality. Personnel at the central storage and testing lab will not know your identity or the volunteer ID assigned to you for the study.

Duke University generally requires that we document in your medical record chart that you are participating in this study. If you do not have a medical record in the DUHS, we will create one for you. The information included in the chart will provide contact information for the research team and information about the risks associated with this study. We will keep this Consent Document in our research files; it will not be placed in your medical record chart.

Some people or groups who receive your health information might not have to follow the same privacy rules. Once your information is shared outside of DUHS, we cannot guarantee that it will remain private. If you decide to share private information with anyone not involved in the study, the federal law designed to protect your health information privacy may no longer apply to the information you have shared. Other laws may or may not protect sharing of private health information.

WHAT ARE THE COSTS TO YOU?

It will not cost you anything to take part in this study. You will not have to pay for any study procedures or study visits.

WHAT ABOUT COMPENSATION?

You will be reimbursed up to $[redacted] for your expenses related to your participation (parking, gas, and time). You will receive $[redacted] for the screening visit, $[redacted] for the vaccination visit, and $[redacted] for each of the follow up in-person visits. You will also receive $[redacted] per visit if additional visits are needed. You will receive compensation for the study activities that are completed.

Payment received as compensation for participation in research is considered taxable income to the research subject. If payment to an individual totals $600 or more in any one calendar year, Duke University is required to report this information to the Internal Revenue Service (IRS). Research subject payments to a non-employee of Duke University adding up to $600 or more during any calendar year will result in a 1099 (Miscellaneous Income) form being issued to the individual and a copy sent to the IRS.

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WHAT ABOUT RESEARCH RELATED INJURIES?

Immediate necessary medical care is available at Duke University Medical Center in the event that you are injured as a result of your participation in this research study. However, there is no commitment by Duke University, Duke University Health System, Inc., or your Duke physicians to provide monetary compensation or free medical care to you in the event of a study-related injury. In addition, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH or the Federal government.

For questions about the study or research-related injury, contact Dr. Walter at (919) 620-5346 during regular business hours and at (919) 970-5720 after hours and on weekends and holidays.

WHAT ABOUT MY RIGHTS TO DECLINE PARTICIPATION OR WITHDRAW FROM THE STUDY?

You may choose not to be in the study, or, if you agree to be in the study, you may withdraw from the study at any time. If you withdraw from the study, no new data about you will be collected for study purposes unless the data concern an adverse event (a bad effect) related to the study. If such an adverse event occurs, we may need to review your entire medical record. All data that have already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

Your decision not to participate or to withdraw from the study will not involve any penalty or loss of benefits to which you are entitled, and will not affect your access to health care at Duke. If you do decide to withdraw, we ask that you contact Dr. Walter in writing and let him know that you are withdrawing from the study.

His mailing address is:
DVTU-RTP
Duke University
PO BOX 106008
Durham, NC 27710

We will tell you about new information that may affect your health, welfare, or willingness to stay in this study.

Your doctor may decide to take you off this study if your condition gets worse, if you have serious side effects, or if your study doctor determines that it is no longer in your best interest to continue. The sponsor or regulatory agencies may stop this study at any time without your consent. Reasons why this might occur include

- You are unable or unwilling to follow the instructions of the study;

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- Participant becomes pregnant prior to study product dosing;
- The study doctor decides that the study is not in your best interest or that you are no longer eligible to be in the study; or
- The study is stopped by the study sponsor, an institutional review board (IRB), or by a government or regulatory agency.

If this occurs, you will be notified and your study doctor will discuss other options with you.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or a research-related injury, or if you have problems, concerns, questions or suggestions about the research, contact Dr. Walter at (919) 620-5346 during regular business hours and at (919) 970-5720 after hours and on weekends and holidays. A member of the study team may also be contacted at (919) 971-5649.

For questions about your rights as a research participant, or to discuss problems, concerns or suggestions related to the research, or to obtain information or offer input about the research, contact the DUHS IRB Office at (919) 668-5111.

STATEMENT OF CONSENT
"The purpose of this study, procedures to be followed, risks and benefits have been explained to me. I have been allowed to ask questions, and my questions have been answered to my satisfaction. I have been told whom to contact if I have questions, to discuss problems, concerns, or suggestions related to the research, or to obtain information or offer input about the research. I have read this consent form and agree to be in this study, with the understanding that I may withdraw at any time. I have been told that I will be given a signed and dated copy of this consent form."

_____	_____	_____
Signature of Subject	Date	Time
_____	_____	_____
Signature of Person Obtaining Consent	Date	Time