Human Immune Responses to an Adjuvanted H5 Vaccine: Durability and Impact of the Seasonal Influenza Vaccine on H5 Induced B Cell Responses

Informed consent date: Sept 19, 2018

NCT03701061

You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University
Consent to be a Research Subject

Title: Human Immune Responses to an Adjuvanted H5 Vaccine: Durability and Impact of the Seasonal Influenza Vaccine on H5 Induced B Cell Responses

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Sponsor: National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH)

Introduction

You are being asked to be in a medical research study. This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

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.

What is the purpose of this study?

The influenza virus (a germ) causes influenza or "flu." The flu is an infection of your breathing tubes and your lungs. Flu is caused by different types of influenza viruses. Flu is spread from person-to-person mainly through coughing and sneezing. When someone has the flu they usually have a runny nose, cough, sore throat, headache and fever. Each winter, the flu causes illness that often feels just like the “common cold.” This is known as “seasonal flu.” Usually the types of influenza viruses are similar from year-to-year.

In recent years, flu viruses that at first only infected birds have begun to infect humans. One of these strains is called avian influenza (A/H5N1 subtype) or “bird flu”. Although no human cases of bird flu have been diagnosed in the United States, this strain has caused severe illness and death in several hundred people since late 2003. Scientists are worried that the A/H5N1 “bird flu” virus could cause a pandemic.

Vaccination is the best way to control flu and prevent its illness and complications. Vaccines help the body to make antibodies that fight infection. When you get the flu vaccine (sometimes called the flu shot), your immune system makes antibodies against the flu virus. If you are exposed to the flu virus after getting the flu shot, the antibodies will help protect you by fighting off the virus.

The purpose of this study is to see how long the immune response to the Influenza A (H5N1) vaccine lasts. The research team wants to explore how the FDA-approved seasonal flu vaccine impacts the immune response in people who were given the pandemic H5N1 vaccine with or without the AS03 adjuvant.

This study plans to enroll up to 50 people, and only those who participated in the HIPC VAX-010 Systems Biology of Influenza A (H5N1) Virus Monovalent Vaccine with and without AS03 Adjuvant study are eligible to take part in this study, regardless of whether they received the H5N1 vaccine with or without the AS03 adjuvant.

In this study, you will be given a single dose of the FDA-approved 2018-2019 seasonal influenza vaccine, Fluarix Quadrivalent. This vaccine is manufactured by GlaxoSmithKline and is recommended for all individuals above 6 months of age. Blood samples will be obtained at each study visit.

Please talk to the study team if you:

- Have been sick in the last 72 hours, including any fever (≥ 100.4 F [≥ 38.0C])
- Have any acute or chronic medical condition
- Have a suppressed immune system as a result of illness, medication, chemotherapy, or radiation therapy
- Are pregnant or breastfeeding or plan to within 1 month
- Have taken corticosteroids within 28 days
- Have a known history of autoimmune disease
- Have a history of Guillain-Barre Syndrome
- Have a history of bleeding disorders
- Have a hypersensitivity or allergy to the vaccine or its components, including egg and latex allergies
- Have a history of any severe reaction to any vaccine
- Have received blood or blood products in the last 3 months or plan to in the next 6 months
- Have received any live virus vaccines within the last 4 weeks or plan to in the next 4 weeks
- Have received any inactivated vaccine within the last 2 weeks or plan to in the next 2 weeks
- Have received any experimental agents in the last 6 weeks or plan to in the next 12 months
- Have received the 2018-2019 influenza seasonal vaccine
- Have had influenza infection during the 2018-2019 influenza season

What will I be asked to do?

The study lasts for about 12 months and requires 7 visits. Visit 1 is the day of the vaccination and the remaining visits occur about 8 days (Visit 2), 15 days (Visit 3), 29 days (Visit 4), 100 days (Visit 5), 180 days (Visit 6), and 365 days (Visit 7) after vaccination. About 5 to 6 tablespoons of blood will be obtained at each study visit. During the study visits we will do the following:

Visit 1 (may take up to 2 hours):

- Obtain your informed consent by explaining the study, answering questions, and signing this document
- Collect your medical history and information about medications
- Measure your oral temperature, pulse, blood pressure, height, and weight
- Do a urine pregnancy test for females of child-bearing potential
- Ask you to agree to use 1 form of birth control for 28 days before and 28 days after getting the vaccine
- Do a targeted physical exam, if needed
- Collect blood samples
- Give you the seasonal influenza vaccine
- Observe you for 20 minutes after getting the vaccine
- Give you a memory aid to record any health changes you have for 7 days after the vaccine

Visit 2 through 7 (may take 30 to 60 minutes):

- Review changes to your medical history and medications
- Do a physical exam and vital signs, if needed
- Collect blood samples
- Review your memory aid (for Visit 2 only)

Optional: Blood Sample Storage for Future Research

This study involves the collection of blood samples. With your agreement, the researchers may store these samples from the study for future medical research. You will be asked to consent separately at the end of this form for the retention and use of your leftover samples.

These samples could be used to further explore the markers of immune response to the AS03 adjuvanted or unadjuvanted H5N1 vaccine and the impact from the seasonal influenza vaccine. Your samples will not be sold or used directly for production of any commercial product. Reports about future research done with your samples will NOT be kept in your health records.

If you do not agree to this future research, your samples will be used only for the study and destroyed after analysis. If consent is not given for use of the samples for future use, you can still participate in the study.

All blood samples collected from you will be stored in secure facilities during the study and will be destroyed on completion of the study analyses. If you have agreed for your samples to be used for future research, then they will be stored indefinitely. You can ask for your samples to be destroyed before this point. However, data derived from samples will continue to be kept and used for the purposes agreed to by you in this document. To ensure privacy, your name and other identifying information will not be attached to the samples released for research purposes or any data derived from your samples; instead, you will only be identified by the subject ID code, which will not allow the lab or third parties to know your identity.

If you decide to leave the study at any time but do not ask for your samples to be destroyed, the researchers may continue to use your samples for the reasons allowed by you in this document.

Optional: Contact for Future Studies & Database Storage

We may want to contact you in the future to see if you are interested in participating in other studies. If and when you are contacted, you can decide then if you want to participate or not in new studies. In order to be able to contact you in the future, we will need to store your information in a secure password protected database. We may contact you about future studies by telephone, e-mail, text or mail. Please note that these methods of communication may not be secure.

The risk to you is a potential loss of privacy; however, your privacy is very important to us and we have safeguards in place to protect your information.

We plan to store in the database selected information including but not limited to the following: your name, gender, date of birth, address, telephone number, e-mail, studies that you either screened for or enrolled in, and health information and sexual orientation so that we can match you with a study that best fits you and contact you in the future. Your decision regarding future contact will not affect your participation in this study.

How will my medicine be provided?

The vaccine that you will receive will be dispensed by the pharmacy and delivered to the study doctor or nurse. The study doctor or a health care provider or nurse on her research team will give the vaccine to you. If you have questions about the vaccine, you should ask the study doctor or study staff.

Who owns my study information and samples?

If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. If you withdraw from the study, data and samples that were already collected may still be used for this study.

What are the possible risks and discomforts?

There may be side effects from the 2018-2019 seasonal influenza vaccine, Fluarix Quadrivalent, that are not known at this time. However, this vaccine is FDA-approved, and is currently being used and recommended for everyone over the age of 6 months to protect against seasonal influenza.

Study vaccine risks:

In adults, the most common (affects more than 1 user in 10) risks and discomforts include local pain (36%), muscle aches (16%), headache (16%), and fatigue (16%). Less common (affects 1 to 10 users in 100) risks and discomforts include arthralgia (8%), gastrointestinal symptoms (7%), shivering (4%), local swelling (2%), local redness (2%), and fever (2%).

Allergic reactions including hives, trouble breathing, or other allergic responses are rare but possible risks, as with any vaccine. Anaphylaxis is an immediate allergic reaction (also known as allergic shock). This type of reaction may include skin rash (hives), swelling around the mouth, throat and eyes, difficulty breathing, sweating, increased pulse, or even fainting. If these reactions occur, they can usually be treated by the study personnel giving emergency medications. Most people who experience anaphylaxis recover completely, but very rarely people can die. Across 4 clinical trials in adults (N=10,923), there was one case of anaphylaxis within one day following Fluarix vaccination.

Guillain-Barré Syndrome (GBS) is a rare disease of the nerves that causes severe weakness and breathing problems. It is a typ of paralysis (where your muscles can't move). Most people who get GBS recover completely, but some people can be paralyzed for a long time or even die. GBS occurs throughout the world, with a median incidence of 1.3 cases/100,000 population (range, 0.4–4.0). While the 1976 swine influenza vaccine was associated with an increased frequency of GBS, evidence on whether GBS is caused by other influenza virus vaccines is unclear. However, this syndrome has not been seen with the more modern influenza vaccine preparations. If influenza vaccine does pose a risk, it is probably slightly more than one additional case per one million people vaccinated.

This vaccine is a killed virus and you cannot get influenza from this vaccine. Just because you received the vaccine does not guarantee that you are protected from seasonal influenza.

Side effects of having blood taken:

Some people may get lightheaded or faint during or just after having blood drawn. Having your blood drawn can be painful and can cause bruising. Bruising can be prevented or reduced by putting pressure on the site for a few minutes after the blood is drawn. It is possible to get an infection where the study staff draw your blood, but this is very rare. To reduce the risk of infection, the study staff will wipe the area clean with alcohol and use sterile equipment.

If you are a woman: to protect against possible side effects of the study drug, women who are pregnant or nursing a child may not take part in this study. If you become pregnant, there may be risks to you, the embryo, or fetus. These risks are not yet known. If you are a woman of childbearing ability, you and the study doctor must agree on at least one method of birth control to use to avoid pregnancy within 28 days before and 28 days after receiving the vaccine. If you think that you have gotten pregnant during the study, you must tell the study doctor immediately. Pregnant women will be taken out of the study.

If you are a man: the effect of the vaccine on sperm is not known.

New Information:
It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Will I benefit directly from the study?
This study is not designed to benefit you directly, but you may receive some level of immune protection from this year's seasonal influenza. However, you may not be fully protected from getting seasonal influenza this year. This study is designed to learn more about the influenza immune response. The study results may be used to help others in the future and may assist researchers in creating a universal influenza vaccine.

Will I be compensated for my time and effort?
You will get compensated for each completed study visit, for your time and effort:

- $75 for Visit 1/ vaccine visit
- $50 for Visits 2 through 7/ follow-up visits

If you do not finish the study, we will compensate you for the visits you have completed. You will get $375 total if you complete all study visits. You may be compensated in the form of cash, check or gift card.

Emory University is required by law to report any payments we make to the IRS. To do this, Emory University Department of Finance needs to keep your Social Security Number on file. You will be asked to fill out a tax form, including your Social Security or Taxpayer Identification Number, in order to be reimbursed, depending on the amount and method of payment. Some payment methods involve mail coming to your house, which may be seen by others in your household. You can decline payment if you are concerned about confidentiality, or you can talk to the study team to see if there are other payment options.

What are my other options?
You do not have to take part in this study. There are seasonal influenza vaccines you can receive outside of this study to protect you against seasonal flu this year.

How will you protect my private information that you collect in this study?
Certain offices and people other than the researchers may look at study records. Government agencies and Emory employees overseeing proper study conduct may look at your study records. These offices include [The Food and Drug Administration, the Office for Human Research Protections, the funder(s), the Emory Institutional Review Board, the Emory Office of Research Compliance]. Study funders may also look at your study records. Emory will keep any research records we create private to the extent we are required to do so by law. A study number rather than your name will be used on study records wherever possible. Your name and other facts that might point to you will not appear when we present this study or publish its results.

Certificate of Confidentiality
There is a Certificate of Confidentiality from the National Institutes of Health for this Study. The Certificate of Confidentiality helps us to keep others from learning that you participated in this study. Emory will rely on the Certificate of Confidentiality to refuse to give out study information that identifies you. For example, if Emory received a subpoena for study records, it would not give out information that identifies you.

The Certificate of Confidentiality does not stop you or someone else, like a member of your family, from giving out information about your participation in this study. For example, if you let your insurance company know that you are in

this study, and you agree to give the insurance company research information, then the investigator cannot use the Certificate to withhold this information. This means you and your family also need to protect your own privacy.

The Certificate does not stop Emory from making the following disclosures about you:

- Giving state public health officials information about certain infectious diseases,
- Giving law officials information about abuse of a child, elderly person or disabled person.
- Giving out information to prevent harm to you or others.

Giving the study sponsor or funders information about the study, including information for an audit or evaluation.

Storing and Sharing your Information

De-identified data from this study, including your de-identified genetic information, may be shared with the research community at large to advance science and health. Data from this study may be placed into public databases where, in addition to having no direct identifiers, researchers will need to sign data use agreements before accessing the data. We will remove or code any personal information that could identify you before your information is shared. This will ensure that, by current scientific standards and known methods, it is extremely unlikely that anyone would be able to identify you from the information we share. Despite these measures, we cannot guarantee anonymity of your personal data.

How is my Genetic Information Protected? What are the Risks?

The Genetic Information Nondiscrimination Act (GINA) is a federal law that generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that GINA does **not** protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, and does not apply to employers with less than 15 employees.

In addition to GINA, the State of Georgia has laws that prohibit insurers from using genetic testing information for any non-treatment purpose. However, like GINA, this state law protection has exclusions: life insurance policies, disability income policies, accidental death or dismemberment policies, Medicare supplement policies, long-term care insurance policies, credit insurance policies, specified disease policies, hospital indemnity policies, blanket accident and sickness policies, franchise policies issued on an insurance policy written as a part of workers' compensation equivalent coverage, or other similar limited accident and sickness policies.

Privilege

In the State of Georgia, in some circumstances your genetic information has may have special legal protections called "privilege." This means that the information cannot be used as evidence in a court. By allowing us to use and disclose your genetic information for this research study along with other information about you that genetic information used in the research may no longer have that legal protection. Other protections described in this form will still apply. There are also other confidentiality protections for research data in general under Georgia state law.

Medical Record

If you have been an Emory Healthcare patient before, then you already have an Emory Healthcare medical record. If you have never been an Emory Healthcare patient, you do not have one. An Emory Healthcare medical record will be made for you if an Emory provider or facility gives you any services or procedures for this study.

Copies of the consent form/HIPAA authorization that you sign will be put in any Emory Healthcare medical record you have now or any time during the study.

The results of some study tests and procedures will be used only for research purposes and will *not* be placed in your medical record. For this study, those items include pregnancy tests.

Tests and procedures done at non-Emory places may not become part of your Emory medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you get ill or injured from being in the study, Emory will help you get medical treatment. Emory has not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Nadine Rouphael at telephone number: (404) 712-1435. You should also let any health care provider who treats you know that you are in a research study.

Costs

There will be no costs to you for participating in this study, other than basic expenses like transportation. You will not be charged for any of the research activities or the study vaccine.

Withdrawal from the Study

You have the right to leave a study at any time without penalty. The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan.

Contact Information

Contact Dr. Nadine Rouphael at 404-712-1370 or the 24 hour emergency phone number at 404-712-1370 during business hours. For evening/weekend hours – 404-686-1000 (Emory Hospital Paging Service, ask for the physician on call for the Hope Clinic, pager number 13068):

- if you have any questions about this study or your part in it,
- if you feel you have had a research-related injury or a bad reaction to the study vaccine, or
- if you have questions, concerns or complaints about the research

Contact the Emory Institutional Review Board at 404-712-0720 or 877-503-9797 or irb@emory.edu:

- if you have questions about your rights as a research participant.
- if you have questions, concerns or complaints about the research.
- You may also let the IRB know about your experience as a research participant through our Research Participant Survey at http://www.surveymonkey.com/s/6ZDMW75.

Consent

Please ***initial*** your choice below for each of the following:

Optional: Blood Sample Storage for Future Use:

_____YES, you may store my unused coded (identified as described above) samples for an indefinite period of time for future research as described above.

_____YES, you may store my unused samples for an indefinite period of time for future research as described above, but you must remove any information that could identify it as mine (labeling it only by study and group). If we remove information that can identify you from the sample, if you decide in the future that you would like to have it removed from research, we will be unable to do so as we will not know which sample is yours.

_____NO, you may not use my samples for other future research. Destroy my unused samples at the end of this study.

Optional: Contact for Future Studies & Database Storage

Please place your initials below (select only ONE option):

_____YES, you may contact me about future studies and store my information in a secure password protected database.

_____ NO, you may not contact me about future studies and store my information in a secure password protected database.

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the study. By signing this consent form, you will not give up any of your legal rights. We will give you a copy of the signed form to keep.

_____

Name of Subject

_____ _____

Signature of Subject (18 or older and able to consent) **Date** **Time**

TO BE FILLED OUT BY STUDY TEAM ONLY

_____

Name of Person Conducting Informed Consent Discussion

_____ _____

Signature of Person Conducting Informed Consent Discussion **Date** **Time**