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STANFORD UNIVERSITY CONSENT TO PARTICIPATE IN A RESEARCH STUDY Response to Influenza Vaccine during Pregnancy

****

Are you participating in any other research studies? _____ Yes _____No

Concise Summary

We are asking your consent in order to participate in a research study. It is very important to know that your participation is entirely VOLUNTARY. The purpose of the study is to better understand the response to the flu vaccine during pregnancy. The study will involve a total of 6 research visits. In the current year when you are pregnant, you will have 3 research visits over a period of 4 weeks. Next year, you will also attend 3 research visits over a period of 4 weeks. At all 6 of the research visits we will draw blood. At the first visit this year and in the fourth study visit (approximately a year from now), you will receive the standard flu vaccine in your arm. The risks of the study are minor including a sore muscle and bruising from the blood draws. The benefit of the study is you will receive protection from the flu but the vaccination is also available through your regular doctor or pharmacy. The researchers hope to better understand the body's response to vaccination so flu vaccines can be improved. The alternative to participating in the study is to not participate and one could get the flu vaccine through a pharmacy or your doctor.

PURPOSE OF RESEARCH

You are invited to participate in a research study on the human immune response. We know immunity to influenza (commonly known as "the flu") appears to be impaired during pregnancy as women are particularly susceptible to flu. We want to investigate what your immune response to a flu shot during pregnancy and then your immune response when you are not pregnant

You were selected as a possible participant in this study because you are a generally healthy pregnant woman between the ages of 18-49 years. You will also continue in the study next year when you are no longer pregnant.

The research study will be conducted at the Stanford Hospital and Clinics. Up to 50 participants will be enrolled.

Participants will complete a total of 6 study visits over 2 flu seasons. During the first visit of each flu season you will receive the injectable flu vaccine as part of this research study.

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Blood will be drawn. The vaccine is licensed by the FDA and is not experimental. This flu vaccine is the standard recommended flu shot and is routinely given to the public during the fall flu season.

The second and third study visits of each flu season will be for the purpose of collecting a small amount of blood to measure your immune response to the vaccination. If you decide to terminate your participation in this study, you should notify Dr. Philip Grant at (650) 723-9443.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you are entitled.

DURATION OF STUDY INVOLVEMENT

Your participation in the study will last for approximately 4 weeks this year and then 4 weeks next year. There are 3 visits during each 4 week period. All the visits will occur at the Stanford Clinical Trials Unit.

PROCEDURES

Dr. Grant and the research study staff will ask you to attend a total of 6 visits:

Year 1 - Clinic Visit 1 (Day 0) The visit will last about approximately 45 minutes to 1 hour.

- Appoximately 1 hour prior to the administration of the routine flu vaccine, you will be given a complete description of the study. After you have reviewed and signed the informed consent, a screening procedure will be done to confirm your eligibility to participate in the study.
- Vital signs (temperature, pulse, blood pressure and respiratory rate) will be obtained and your height and weight will also be measured and recorded. If you have a fever or you are sick, you cannot be enrolled at this visit but may be asked to return at a later time once your illness is resolved.
- We will collect your medical history including history related to your current and past pregnancies.

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- Approximately 4 tablespoons of blood will be collected from a vein in your arm to assess your baseline immune function as well as to check your hemoglobin if this has not been performed as part of your routine clinical care.
- You will then receive the flu shot (this may occur either in the Ob/Gyn clinic as part of your routine clinical care or in our research clinic).

Clinic Visit 2 (approximately 7 days after vaccination) The visit will take approximately 15 minutes.

- Approximately 4 tablespoons of blood will be collected from a vein in your arm.
- Any changes to your medications and changes in your health will be reviewed.

Clinic Visit 3 (approximately 28 days after vaccination) The visit will take approximately 15 minutes.

- Approximately 4 tablespoons of blood will be collected from a vein in your arm.
- Any changes to your medications and changes in your health will be reviewed.

Year 2 - Clinic Visit 4 (Approximately 1 year after first research visit) The visit will last about approximately 30 minutes.

- Study eligibility will be reviewed and all your questions will be answered before any study procedures are started.
- Vital signs (temperature, pulse, blood pressure and respiratory rate) will be obtained and your weight will also be measured and recorded. If you have a fever or you are sick, you will may be asked to return at a later time once your illness is resolved.
- Approximately 4 tablespoons of blood will be collected from a vein in your arm to assess your immune function prior to vaccination.
- Any changes to your medications and changes in your health will be reviewed.
- You will be given a flu vaccination with the inactivated version of the flu vaccine.

  You will be observed in the clinic for 15 minutes following vaccination to monitor and treat any serious allergic reactions, should they occur. During that time, we will ask you a few questions, such as any updates of your medical history and new medications

Clinic Visit 5 (7 days after second vaccination) The visit will take approximately 15 minutes.

- Approximately 4 tablespoons of blood will be collected from a vein in your arm.

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- Any changes to your medications and changes in your health will be reviewed.

Clinic Visit 6 (28 days after second vaccination) The visit will take approximately 15 minutes.

- Approximately 4 tablespoons of blood will be collected from a vein in your arm.
- Any changes to your medications and changes in your health will be reviewed.

Tissue Sampling for Research

Research using tissues is an important way to try to understand human disease. You have been given this information because the investigators want to include your blood in an immunology research project and because they want to save the samples for future research. There are several things you should know before allowing your tissues to be studied.

Your blood samples will be stored using a unique study identification number. The results of the study of your samples will be used for research purposes only and you will not be told the results of the tests.

Your samples will be analyzed and stored at Stanford University and by other researchers at Stanford and outside of Stanford, including colleagues participating in the Cooperative Center for Human Immunology (CCHI) and Human Immunology Project Consortium (HIPC) funded through the National Institutes of Health (NIH). Your samples will be identified by your unique study ID code and study visit number. Your name will not be associated with any samples used for future research, but they may be identified by your age. **By signing this consent form and agreeing to participate in the study, you agree to the use of your samples for future research.**

Tissue Sampling for Immunity-Related Genetic Testing

As part of the analysis on your samples, the investigators will do immunity-related genetic testing. Genetic research is research that studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications and responses to treatment such as the flu vaccine. Genetic testing will be performed on coded specimens. Your name will not be associated with any samples used for future research, but they may be identified by your age.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information

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Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

The results from the study of your research samples will be used for research purposes only and you will not be told the results of the tests. Your samples will be analyzed and stored at Stanford University and outside of Stanford, including the National Institutes of Health, sites participating in the Human Immunology Project Consortium (HIPC) and/or by other research colleagues. The goal of this research is to discover genetic factors that contribute to the prevention or treatment of illnesses.

Genetic information from analyses of your coded samples and a portion of your coded medical information may be stored in one of the National Institutes of Health (NIH) databases such as the NIH HIPC data repository (ImmPORT) and the National Center for Biotechnology Information databases (NCBI). These research results along with information from other research participants will be used for future research. These databases will be accessible by the Internet. Only anonymous information from the analyses will eventually be put in a completely public research database, available to anyone on the Internet.

No traditionally-used identifying information about you, such as your name, address, telephone number, or social security number, will be put into the public database. While the public database will not contain information that is traditionally used to identify you, people may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you.

However, your privacy is very important to us and we will use safety measures to protect it. Despite all of the safety measures that we will use, we cannot guarantee that your identity will never become known.

PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the Protocol Director and study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact your treating physician or research study staff to reschedule as soon as you know you will miss the appointment.

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- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you may have during your participation in the research study.
- During Year 2 of the Study, tell the Protocol Director or research staff if you believe you might be pregnant.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

If you are coming in-person to research visits, you are required to be fully vaccinated—2 doses (1 for Johnson and Johnson), 2 weeks out and to provide proof of your vaccination (e.g., CDC COVID-19 Vaccination Card, e-Health record, etc.) to the researcher prior to study participation. Alternately, you can provide a negative COVID test within 72 hours of your visit.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled.

If you decide to stop your participation in this study, you should notify Dr. Philip Grant at (650) 723-9443. The following information will be collected if possible:

- We will ask about your current health status and note any changes since the previous visit.
- You will be encouraged to allow follow-up of any safety-related health events.

The Protocol Director may also withdraw you from the study without your consent for one or more of the following reasons:

- Failure to follow the instructions of the Protocol Director and research staff,
- The Protocol Director decides that continuing your participation could be harmful to you,
- A new pregnancy during the second year,
- You need treatment not allowed in the study,
- The study is cancelled,
- Other administrative reasons, and
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

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There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions.

- The discomforts of this study are those of receiving IM injection and blood drawn from an arm vein, and possible reactions to the vaccine. Drawing blood causes transient discomfort and may cause fainting. Infection at the site where blood will be drawn or where the vaccination is given is extremely unlikely but is a potential risk. Bruising at the site of blood drawing may occur, but can be prevented or lessened by applying pressure for several minutes immediately after the blood draw.
- Immediate allergic reactions to vaccine, including anaphylaxis, are extremely rare (approximately 1 person in 4,000,000), and might occur as a skin rash such as hives, difficulty breathing, fainting, drop in the blood pressure and death. Such reactions can usually be stopped by emergency medications administered by study personnel.
- Vaccine recipients may develop systemic reactions such as fever, headaches, body aches, and fatigue. These reactions are usually greatest within the first 24 to 72 hours after vaccination and last 1 to 2 days. Analgesics (*e.g.*, aspirin or Tylenol®) and rest will generally relieve or moderate these symptoms. Other hypersensitivity reactions, including Arthus reactions resulting in large local swelling reactions, are also possible.
- Although Guillain-Barré syndrome may have been associated with the 1976-77 inactivated swine influenza vaccine and TIV vaccines used in early 1990's, subsequent inactivated vaccines have not been associated with an increased risk of this condition.
- Participation in this study may involve risks to the participant which are currently unforeseeable.

POTENTIAL BENEFITS

- There are no benefits to you for participating in this study other than receiving the seasonal influenza vaccine, which is available publicly.
- Participants given the seasonal influenza vaccine are likely to experience decreased frequency and severity of subsequent influenza infection. The beneficial role of influenza vaccination has been recognized increasingly over the past several years as more information has become available about the high rate of morbidity and mortality from this respiratory pathogen.
- WE CANNOT AND DO NOT GUARANTEE OR PROMISE THAT YOU WILL RECEIVE ANY BENEFITS FROM THIS STUDY.

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ALTERNATIVES

The alternative to participating in this study is to not participate in this study

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. If you decide not to participate, tell the Protocol Director.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

ClinicalTrials.gov

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.

CONFIDENTIALITY

The results of this research study may be presented at scientific or medical meetings or published in scientific journals. Your identity and/or your personal health information will not be disclosed except as authorized by you or as required by law. However, there is always some risk that even de-identified information might be re-identified

The purpose of this research study is to obtain information on the immune response to the seasonal influenza vaccination during pregnancy. The results will be provided to the sponsor, the Food and Drug Administration and other federal and regulatory agencies as required.

Identifiers might be removed from identifiable private information and/or identifiable specimens and, after such removal, the information and/or specimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as

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evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you 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.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law such as child abuse and neglect, or harm to self or others.

Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

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Authorization To Use Your Health Information For Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?
This is a research study on immune development. We want to see what your response to a flu immunization looks like during pregnancy and when you are not pregnant.

As part of this research you will be asked questions about your personal health information such as age, race/ethnicity, vaccination history and health history. We are collecting this information to see if these factors also affect immune development. Your health information will be kept on a password-protected, encrypted computer and affiliated researchers will have access to de-identified information.

The results will be provided to regulatory agencies as required. The results of this research study may be presented at scientific or medical meetings or published in scientific journals. However, your identity (except for age) will not be disclosed.

Do I have to sign this authorization form?
You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study. Signing the form is not a condition for receiving any medical care outside the study.

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If I sign, can I revoke it or withdraw from the research later?

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to:

Dr. Philip Grant
Stanford-LPCH Vaccine Program
Stanford University School of Medicine
1000 Welch Road, Suite 202
Palo Alto, CA 94304-5350

What Personal Information Will Be Obtained, Used or Disclosed?

Your health information related to this study, may be used or disclosed in connection with this research study, including, but not limited to, contact information for appointment reminders (name, telephone number, address, email), for clinic registration (date of birth, age, race and ethnicity, gender, medical record number), information necessary to process study reimbursements (social security number), influenza vaccination history, medication history, health history, and results from tissue assays used for immune-related research. Results from research assays will be labeled with your Study ID and visit number, and your identity (except for age) will not be disclosed. Future use of your samples for research, including genetic testing, will be performed on coded specimens. The NIH Human Immunology Project Consortium (HIPC) data repositories (ImmPORT) will store the results of the research assays results. Genetic data that is developed in this study will be made available to other researchers through the National Center for Biotechnology Information (NCBI) databases.

In the event that you have a change in your health status related to the study procedures and are hospitalized or seen at Stanford University

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Hospital and Clinics, the research staff may access those medical records to evaluate the unanticipated event.

Who May Use or Disclose the Information?
The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director, Philip Grant, MD
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary
- Other physicians, researchers, nurses, study coordinators and clinical research assistants who are members of the study team
- The Stanford Hospital and Clinics and Clinical and Translational Research Unit staff.

Who May Receive or Use the Information?
The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- The National Institutes of Health (NIH)
- The Food and Drug Administration (FDA)
- The study biostatisticians
- National Center for Biotechnology Information (NCBI)
- Research colleagues at Stanford University and outside of Stanford including colleagues within the NIH Cooperative Center for Human Immunology (CCHI) and Human Immunology Project Consortium (HIPC) funded through the National Institutes of Health (NIH). Your information will be coded and you will not be identified by name. Your age may be disclosed.

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?
Your authorization for the use and/or disclosure of your health information will end on December 31, 2065 or when the research project ends, whichever is earlier.

_____ _____
Signature of Participant Date

_____
Print Name of Participant

Participant ID:

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FINANCIAL CONSIDERATIONS

Payment

You will receive $50.00 for each regularly scheduled study visit you complete. If you complete the 3 annual visits, you will receive a total of $150 for each year of participation. Payments may only be made to U.S. citizens, legal resident aliens, and those who have a work eligible visa. You may need to provide your social security number to receive payment.

Costs: There is no cost to you for participating in this study, other than basic expenses like transportation and the personal time it will take to come to all of the study visits.

Sponsor: The National Institutes of Health are providing financial support and/or material for this study, as well as some financial support for the facility and staff where part or all of the study is taking place.

COMPENSATION for Research-Related Injury

All forms of medical diagnosis and treatment – whether routine or experimental – involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you in obtaining appropriate medical treatment. In the event that you have an injury or illness that is directly caused by your participation in this study, reimbursement for all related costs of care first will be sought from your insurer, managed care plan, or other benefits program. **You will be responsible for any associated co-payments or deductibles as required by your insurance.**

If costs of care related to such an injury are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, the Protocol Director will assist you in applying for supplemental benefits and explain how to apply for patient financial assistance from the hospital.

You do not waive any liability rights for personal injury by signing this form.

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CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Philip Grant, MD, at (650) 723-9443. You should also contact him at any time if you feel you have been hurt by being a part of this study.

Appointment Contact: If you need to change your appointment, please contact the Research Study Team at 650-724-5551.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, 1705 El Camino Real, Palo Alto, CA 94306.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form

- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you about future studies that may be of interest to you?

____ Yes ____ No

What type of appointment reminder would you like to receive from us (**choose one**)?

_____ Telephone call/voice mail

_____ Email (will not use secure encrypted email; please do not reply to the reminder with any private or confidential health information)

Signing your name means you agree to be in this study and that you were given a copy of this signed and dated consent form.

_____ _____
Signature of Adult Participant Date

_____
Print Name of Adult Participant

_____ _____
Signature of Person Obtaining Consent Date

_____
Print Name of Person Obtaining Consent

Participant ID:

The following witness line is to be signed only if the consent is provided as a summary form and accompanied by a short form foreign language consent.

_____ _____
Signature of witness Date

(e.g., staff, translator/interpreter, or family member)

_____
Print Name of Witness

- *Translated short form must be signed and dated by both the participant (or their LAR) AND the witness.*
- *The English consent form ("summary form"):*
  - *Must be signed by the witness AND the Person Obtaining Consent (POC).*
  - *The non-English speaking participant/LAR does not sign the English consent.*
  - *The non-English speaking participant/LAR should not sign the HIPAA participant line*

If the participant or the LAR is non-English speaking, the Person Obtaining Consent (POC) must ensure that 1) the LAR's Description of Authority is completed and 2) that any questions or options presented by the consent form are documented and initialed by the POC on the Summary Form, per the participant's wishes, as they are understood during the consent process.