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Medical College of Wisconsin
INTRODUCTION TO THE INFORMED CONSENT

Prospective analysis of immunogenicity of the nanovalent human papillomavirus vaccination (GARDASIL 9) in patients pre and post solid organ transplant

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Definitions

Human Papilloma Virus (HPV) – is the most common sexually transmitted infection in the United States. HPV is responsible for causing nearly all cervical cancers and most vaginal, vulvar, anal, rectal, penile, and oropharyngeal cancers.

Gardasil-9 – a vaccine that is FDA approved for the prevention of HPV

Antibodies – proteins in the blood produced by your immune system in response to the presence of an outside substance (vaccine, bacteria, etc.)

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Purpose

This project is being done to compare the effectiveness of the GARDASIL-9 vaccine in patients with compromised immune systems.

Length

- You will be in this research project for about 3 years.
- We would also like to follow up with you by phone for up to 10 years after your last research visit.

Procedures

Subjects will be assigned to receive the GARDASIL-9 vaccine either 6 months before or 6 months after they undergo kidney transplant.

List of visits:

- Screening and Enrollment
  - Total Number: 1 or 2
  - Total Time: 1-2 hours
- Treatment
  - Total Number: 3
  - Total Time: 1 hour
- Follow up
  - Total Number: 3
  - Total Time: 30 minutes each

Procedures that will occur at various visits:

Invasive Procedures

- Vaccine injection, blood draws

Non-invasive Procedures

- Medical history, phone calls

Risks

This is a brief list of the most commonly seen side effects. The ***full consent form*** after this introduction contains a more complete list of potential research risks.

GARDASIL-9 risks:

- Pain, swelling, redness, itching, bruising, bleeding, and/or a lump where you got the shot
- Headache
- Fever
- Nausea
- Dizziness
- tiredness
- Diarrhea
- Abdominal pain
- Sore throat
- Fainting

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Benefits

We don't know if this project will help you. Your condition may get better but it could stay the same or even get worse.

My Other Options

You do not have to join this project. Your other options may include:

- Joining a different project
- Getting no treatment for this condition

If you have more questions about this project at any time, you can call Dr. Denise Uyar at 1-855-771-9477.

If you have questions about your rights as a participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

CONSENT TO PARTICIPATE IN RESEARCH

A1. INTRODUCTION – WHY ARE WE ASKING YOU TO PARTICIPATE?

You are being invited to participate in this research because you are scheduled to receive a kidney transplant. Because of your condition, you may be eligible for a research project examining how your immune system responds to a vaccine for human papilloma virus (HPV) known as GARDASIL-9.

A total of about 100 people are expected to participate in this research at the Medical College of Wisconsin/Froedtert Hospital.

The Director of the project is Dr. Denise Uyar in the Department of Obstetrics and Gynecology. A research team works with Dr. Uyar. You can ask who these people are.

The Medical College of Wisconsin will be paid by the Sponsor, Merck & Co., Inc., for carrying out this project.

A2. DO I HAVE TO PARTICIPATE?

You can decide whether to take part in this research or not. You are free to say yes or no. If you do not agree to join, or if you leave, you will not be penalized or lose any benefits that you had before starting the research project. Even if you join this project, you do not have to stay in it. You may stop at any time. Take as much time as you need to make your choice.

A research project is different from routine medical care in three ways: 1) there are extra risks that we will tell you about in this form; 2) you may have some extra medical tests and visits; 3) the research procedures, tests and visits follow a set plan that must be kept.

A3. WHY IS THIS PROJECT BEING DONE?

HPV is responsible for nearly all cervical cancers as well as some cancers affecting the back of the throat (oropharyngeal), anal cancers, vulvar cancers, penile cancers and vaginal cancers. Individuals with immune suppression are at particularly high risk for HPV infections. GARDASIL-9 is a vaccine that is U.S. Food and Drug Administration (FDA) approved to prevent infection with the 9 strains of HPV which may decrease incidence of these types of cancers. This vaccine has been FDA approved since 2006 and is available by prescription.

In this study, we want to learn how people with suppressed immune systems (e.g.-those undergoing an organ transplant) respond to this vaccine. We plan to study people who receive the vaccine before they undergo a kidney transplant and those who receive the vaccine after they undergo a kidney transplant to document the difference in the immune response to the vaccine compared to people who are not immune suppressed.

B1. WHAT WILL HAPPEN IF I PARTICIPATE?

Research groups
This study has two groups:

- Subjects who will receive the GARDASIL-9 vaccine before they undergo a kidney transplant

- Subjects who will receive the GARDASIL-9 vaccine after they undergo a kidney transplant

You will be assigned to one of these two groups based on whether you have already had your kidney transplant or not (e.g. if you have already undergone your kidney transplant, you will be assigned to the group that will receive the vaccine after transplant).

We will check both groups' blood at different time points during the study to see how much of an immune response their body has to the vaccine. We will compare the results of the two groups with each other and with people who are not immune suppressed.

Screening procedures:
If you decide to join and sign this consent form, a member of the study team will ask you some questions about your health and medical history.

If the screening information shows that you meet the requirements, then you will be able to continue in the study. If the screening information shows that you cannot be in the research, the research doctor will discuss other options with you and/or refer you back to your regular doctor.

The following tests and procedures will only occur if you are eligible to participate, you agree to participate, and you sign this consent form.

Summary of Procedures:
The GARDASIL-9 vaccine will be administered by needle injection into a muscle in either the upper arm or thigh. This vaccine requires 3 doses over the course of 6 months. Depending on what group you are assigned to, you will either receive this vaccine series before or after your kidney transplant.

The schedule of administration will be:
- Dose 1
- Dose 2 (2 months after dose 1)
- Dose 3 (6 months after dose 1)

Regardless of what group you are assigned to, you will have the following tests and procedures:

Blood tests-blood will be drawn by a trained nurse or clinician from a vein in your arm at the following time points:
- Before your first dose of the vaccine – a total of about 15 mls (1 tablespoon) of blood will be drawn for the following tests
    - Geometric Mean Titer (GMT) – a test of the concentration of HPV antibodies in your blood
- 7, 12, and 24 months after your last dose the vaccine – a total of about 15 mls (1 tablespoon) of blood will be drawn at each visit to see how much of a response your immune system has had to the vaccine.
    - Geometric Mean Titer (GMT) – a test of the concentration of HPV antibodies in your blood

Phone calls – you will be contacted by phone by a member of the study team to check in on your condition and to ask about any changes in your health 72 hours after each dose of the vaccine.

At every visit after enrollment, you will also be asked some questions about your transplant status, any side effects you may be experiencing, and what medications you are taking.

The blood collected for this part of the project will be coded, which means it will be labeled with numbers and/or letters instead of information that could identify you. Only the research team will be able to link the code to you. The research team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you.

B2. HOW LONG WILL I BE IN THE PROJECT?

You will be in this research project for about 2 years. You will receive the vaccine in 3 shots over the course of approximately 6 months.

We may continue to monitor your health by looking at your medical records and may contact you annually by phone for up to 10 years after your last research visit to monitor for HPV infection related health problems.

B3. CAN I STOP BEING IN THE PROJECT?

You are free to withdraw from the project at any time. If you leave, your regular medical care will not change. If you are thinking about leaving, please tell the research doctor.

The research doctor can tell you about the effects of stopping, and you and the research doctor can talk about what follow-up care would help you the most.

The research doctor may take you out of this project at any time. This would happen if:

- They think it is in your best interest.
- You do not follow the project rules.
- The whole project is stopped.

If this happens, the research doctor will tell you.

B4. ARE THERE ANY SPECIAL INSTRUCTIONS WHILE I AM IN THE PROJECT?

- You should tell the doctor about any medicines you are taking including over the counter and supplements.
- Do not participate in any other research study without first contacting Dr. Uyar.

C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE PROJECT?

There are risks to taking part in any research project. There is a risk that you may get a drug (vaccine) not help your condition or may make it worse. There also may be problems (side effects) we do not know about yet, If we learn about new important side effects, we will tell you. A similar HPV vaccination (quadrivalent HPV) has been administered in the solid organ

transplant population previously, and no additional safety signals were reported in association with the vaccine.

We watch everyone in the project for problems (side effects). **You need to tell the research doctor or a member of the research team immediately if you experience any problems, side effects, or changes in your health.** In an emergency, call 911.

C2. RISKS OF GARDASIL-9 VACCINE

The vaccine itself may cause problems (side effects). Side effects may be mild or very serious. Some can last a long time or never go away. Most go away within a few days after you receive the vaccine.

The side effects that other people have experienced so far with the vaccine are:

- Pain, swelling, redness, itching, bruising, bleeding, and/or a lump where you got the shot
- Headache
- Fever
- Nausea
- Dizziness
- tiredness
- Diarrhea
- Abdominal pain
- Sore throat
- Fainting - Fainting can happen after getting GARDASIL 9. Sometimes people who faint can fall and hurt themselves. For this reason, your health care professional may ask you to sit or lie down for 15 minutes after you or your child get GARDASIL 9. Some people who faint might shake or become stiff.

Tell the health care professional if you have any of these problems because these may be signs of an allergic reaction:

- difficulty breathing
- wheezing (bronchospasm)
- hives
- rash

C3. OTHER RISKS OF THIS RESEARCH PROJECT

Risks of blood draws

- There may be pain, swelling, or bruising around the vein where your blood is drawn.
- You may feel dizzy, or you may faint.
- Infection, though rare, may occur from where the blood is taken.

Another risk may be loss of confidentiality. Every effort will be made to keep your research records confidential but we cannot guarantee it. Depending on the kind of information being collected, if your research information were accidentally seen, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the project director about whether this could apply to you.

C4. REPRODUCTIVE RISKS

Risks to subjects who could become pregnant
We do not know if the vaccine causes harm to a baby, so we do not want anyone who might be pregnant to enter the project.

You should not become pregnant or nurse a baby while in this project. You must tell the research doctor right away if you think you are pregnant.

If you become pregnant during the project, you will be withdrawn from participation for safety reasons. If you become pregnant while you are taking this vaccine, we ask that you inform the research doctor immediately. The research doctor will ask you for written permission to obtain information from you or your obstetrician on your pregnancy and the health of the baby.

C5. ARE THERE ANY BENEFITS TO TAKING PART IN THE PROJECT?

Receiving the full series of the GARDASIL-9 vaccine reduces the risk of contracting HPV which may lower your risk of developing various cancers. The information we learn will also help investigators learn more about the effectiveness of the GARDASIL-9 vaccine in immunocompromised individuals.

D1. ARE THERE ANY COSTS TO BEING IN THE PROJECT?

Most of the medical care that you will receive in this project is considered routine care for your condition and would be recommended whether or not you join the project. Costs for routine care will be billed to you or your insurance carrier. For routine clinical care, you will be responsible for paying any copayment, coinsurance, or deductible that is required by your insurance carrier. Activities / costs that are part of the project will not be billed to you or your insurance company. These include: research only blood draws. Some insurers will not pay for drugs, tests or hospitalization that are part of research, so check with your insurer before you join this project. If you have questions regarding costs, please contact Dr. Uyar.

If you participate in this research, the costs of any necessary emergency medical treatment in the event of a research-related injury will be billed to you or your health insurance.

D2. WILL I BE PAID FOR PARTICIPATING IN THE PROJECT?

You will receive $25 for each visit that takes place outside of your regular care visits (up to 9 visits and up to a total of $225). To pay you, we need to collect your social security number. Any payment may be reportable as income on your taxes.

Dr. Uyar, other researchers, or research companies may patent or sell products, discoveries and data or information that result from this research. Dr. Uyar or Froedtert/MCW will not pay you if this happens. You will not receive any payment or commercial rights for products, data, discoveries, or materials gained or produced from your health information or blood.

D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this project. You are free to say yes or no. If you do not join this project, your research doctor can discuss other healthcare choices with you.

The GARDASIL-9 vaccine is available without being in any research project.

The research doctor can explain both the possible benefits and the risks of other options that are available to you.

D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE PROJECT?

If we learn any important new information about GARDASIL-9 that might change your mind about being in the project, we will tell you about it right away. You can then decide if you want to stay in the project.

When research data/biospecimens are collected and analyzed, there is the chance of finding something clinically relevant. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as feeling worried about a finding for which no treatment is required or appropriate).

The results from the data/biospecimens we collect in this research study are not the same quality as what you would receive as part of your health care, so you will not be informed of any clinically relevant research findings. The results of your research data/biospecimens will not be placed in your medical record.

D5. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE PROJECT?

Emergency medical treatment for injuries directly related to your participation in this research project will be provided to you. You or your health insurance will be billed for the costs of this emergency treatment. MCW will decide on a case by case basis if they will reimburse you or your insurer for emergency treatment costs. If your research-related injury requires medical care beyond this emergency treatment, you or your insurer will be responsible for the costs of this follow-up care.

At this time, there is no plan for any additional financial payments.

If you believe that you have been injured because of your participation in this project, contact the research doctors right away. Contact information: Dr. Uyar, 1-855-771-9477.

Nothing in this consent form affects any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE PROJECT?

- If you have more questions about this project at any time, you can call Dr. Uyar at 1-855-771-9477.
- If you have questions about your rights as a research participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

E1. What health information will be collected and used for this project?

To be in this research project, the research team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the project. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the project.

The protected health information (PHI) originates from services you will or have received at one or more of the following locations: the Medical College of Wisconsin (MCW); Versiti, Inc.; Children's Hospital of Wisconsin (CHW); any Froedtert Health Affiliate- Froedtert Hospital (FH), Inc.; Froedtert Menomonee Falls Hospital; Froedtert West Bend Hospital; Froedtert & The Medical College of Wisconsin Community Physicians Clinics, Inc. (FMCWCP); the West Bend Surgery Center, LLC; and the Froedtert Surgery Center, LLC.

The health information to be collected and used for this project is:

- Medical history for determining eligibility
- Medical records of the care you receive for this project
- Medical records dating from when you join this project until up to 10 years after your last study visit

E2. Who will see the health information collected for this project?

The only MCW/Froedtert Hospital employees allowed to handle your health information are those on the research team, those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

If the costs of any necessary emergency medical treatment in the event of a research-related injury are billed to your health insurance, your health information may need to be disclosed to the insurer for billing purposes.

The research team may share your information with people who don't work at MCW/Froedtert Hospital because they planned, pay for, or work with us on this project. The federal Privacy Rule may no longer protect your health information once it leaves MCW/Froedtert Hospital. For this project, we plan to share information with those doctors, researchers or government representatives working with us on this project at the institutions or companies listed here:

- Q2 Solutions, Indianapolis, IN
- Merck & Co., Inc., Rahway, NJ

Because this project involves the use of drugs and/or devices, the FDA also has the right to inspect all project records.

We may record your research information, including results of tests and procedures done for research, in your Froedtert Hospital and/or Medical College of Wisconsin medical record. As a result, this research information may be seen by people allowed to see your medical records for healthcare operations or treatment, by those you allow to see your medical records by giving written permission, and by others when required by law.

We will not use your personal health information for a different project without your permission or the permission of a hospital research review board (IRB). Once all personal identification is removed from your health information and/or biospecimens, the information and/or biospecimens may be used for future research or distributed to another investigator for future research without additional informed consent from you or your legally authorized representative. The information might also be used or released for other purposes without asking you. Results of the project may be presented in public talks or written articles, but no information will be presented that identifies you.

E3. What are the risks of sharing this health information?

One risk of taking part in a research project is that more people will handle your personal health information collected for this project. The research team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. If you have questions, you can talk to the research doctor about whether this could apply to you.

E4. How long will you keep the health information for this project?

If you sign this form, we plan to keep your information without any end date in case we need to check it again for this project.

E5. Can I cancel my permission to share this health information?

If you change your mind later and do not want us to collect or share your health information, you need to send a letter to Dr. Denise Uyar at:

Department of Obstetrics and Gynecology
Medical College of Wisconsin
9200 W Wisconsin Ave
Milwaukee, WI 53226

The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we will decide that you cannot continue to be part of the project. We may still use the information we have already collected.

CONSENT TO PARTICIPATE

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document.
- All of my questions have been answered to my satisfaction.
- The project's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the research team use and share the health information and other information gathered for this project.
- I voluntarily agree to participate in this research project. I agree to follow the procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

Subject's Name *please print*	**Subject's Signature**	**Date**

Name of Witness, if applicable *please print*	**Signature of Witness**	**Date**
Rationale for Use of Witness ☐ Subject has limited/no literacy ☐ Subject has limited English proficiency ☐ Subject has limited/no vision	☐ Sponsor requirement ☐ Other _____	

Name of person discussing/ obtaining consent *please print*	**Signature of person discussing/obtaining consent**	**Date**