Duke University Health System

Safety of Simultaneous Vaccination with Zoster Vaccine Recombinant (RZV) and Quadrivalent Adjuvanted Inactivated Influenza Vaccine (allV4) (Lead)

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Consent to Participate in a Research Study

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CONCISE SUMMARY

The purpose of this study is to compare the safety of administering Shingrix® at the same time as FLUAD™ or Fluzone® High-Dose in older people. Shingrix® and FLUAD™ both contain novel adjuvants, which are substances added to each of these vaccines to improve their immune response and effectiveness.

As part of this study, you will be asked to come in for 3 study visits and you will receive 4 scheduled phone calls over approximately 3 1/2 months. You will have about 3 teaspoons of blood drawn at 2 of the study visits.

Some risks associated with this study include momentary discomfort and/or bruising from blood drawing. You may experience pain, redness or bruising at your injection site, following vaccination. The risks of the vaccines are explained in more detail later in this consent form. You would experience the same risks from the vaccines whether or not you participate in this study. It is unknown if giving these two vaccines at the same time will result in more or worse side effects. A potential benefit is getting the recommended vaccines and at the same time.

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

You are being asked to take part in this research study because you are at least 65 years old and you are interested in receiving a shingles vaccine and a seasonal flu shot. Research studies are voluntary and include only people who choose to take part. Please read this consent form carefully and take your time making your decision. As your study doctor or study staff discusses this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. We encourage you to talk with your family and friends before you decide to take part in this research study. The nature of the study, risks, inconveniences, discomforts, and other important information about the study are listed below.

Please tell the study doctor or study staff if you are taking part in another research study.

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Through a contract from the Centers for Disease Control and Prevention (CDC), the CDC will support this research study. The CDC will pay a portion of Dr. Kenneth Schmader's and Dr. Emmanuel Walter's and their research team's salaries to conduct the study.

WHO WILL BE MY DOCTOR ON THIS STUDY?

If you decide to participate, Dr. Kenneth Schmader 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 work by causing the body to make proteins called antibodies that fight infection. Vaccination is the most effective way to prevent infections such as shingles and influenza (flu). The Advisory Committee on Immunization Practices (ACIP) currently recommends Shingrix®, a vaccine for the prevention of herpes zoster (HZ) or shingles in older adults, and influenza vaccination for older persons to prevent influenza and its complications. Shingles is characterized by a rash and pain, which can last for months or even years, affecting quality of life in older persons. Flu infections in older people are more likely to cause serious complications or death.

The purpose of this study is to compare the safety of administering Shingrix® at the same time as FLUAD™ or Fluzone® High-Dose in older people. Shingrix® and FLUAD™ both contain novel adjuvants, which are substances added to each of these vaccines to improve their immune response and effectiveness. We hope to gain additional knowledge related to administering two vaccines with novel adjuvants at the same time. These vaccines are all approved by the Food and Drug Administration (FDA) for use in older people.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?

Approximately 400 adults who are at least 65 years old will be enrolled in this study, with approximately 220 adults to take part at Duke.

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WHAT IS INVOLVED IN THE STUDY?

If you agree to be in this study, you will be asked to sign and date this consent form. If you do not sign this consent form, you will continue to receive care, but not as a part of this study. Refusal to participate will involve no penalty or loss of benefits.

Visit 1 (clinic visit) Study Day 1 (1 ½ to 2 hours):

Study staff will explain the study, review the consent form with you, and answer any questions you may have. You will then read, sign and date the consent form. Your medical history, medications that you are currently taking, as well as study criteria will be reviewed, to make sure that you qualify for the study. You will be asked to complete a brief assessment, including a memory test and a measure of your physical activity. Study staff will take your temperature, blood pressure, and heart rate. You will be asked about your history of flu vaccination and shingles vaccination, and will you be asked about any pain, swelling, or redness you are experiencing in your arm before vaccination. A blood sample of 15 mL (3 teaspoons) will be taken to test for antibody levels. You will be randomly assigned (like flipping a coin) to receive Shingrix® and either the FLUAD™ or Fluzone® High-Dose flu vaccine. You will not be told which flu vaccine you are receiving. You will be given the Centers for Disease Control and Prevention (CDC) Flu Vaccine Information Statement for your records.

The vaccines will be administered by licensed study staff. You will need to stay in the clinic for at least 15 minutes after vaccination to be watched for any reactions. While you are still in the clinic, you will be asked about any pain you feel where you received your shot. You will be asked how you are feeling, and if you have developed any bothersome symptoms after receiving the flu shot. Study personnel will look at your arm and the site of the injection before you leave the clinic. You will be given a symptom diary form, a measurement tool, and a digital thermometer, and shown how to use them for the study. You will be asked to write down your temperature and any symptoms that you have daily (every day), beginning on the evening of the day you got the vaccine to seven days after you receive the shot (total of 8 days). You should also write down any new medicines or change in medicine dose that you take during this time, even over-the-counter medicines like Tylenol® (acetaminophen or paracetamol). You will also be asked to measure (with the measurement tool) the spot where you received your shot if the area gets red or swollen.

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You should contact the study staff if you have any severe reactions (explained on the daily symptom diary form you will receive) in the week after receiving the shingles and flu vaccines.

Visit 2 (phone call or text message) Study Day 4 (1-2 minutes):
A member of the study team will call, email, or text to remind you to complete the diary entries. How they contact you is your choice.

Visit 3 (phone call) Study Day 9 (15-30 minutes):
A member of the study staff will contact you to review the information about your symptoms and medications that you should have been recording daily in the symptom diary. We will also ask if you received any medical attention other than a routine visit.

Visit 4 (clinic visit) Study Day 29 (15-30 Minutes):
About 28 days after the first visit, you will return to the research clinic for another in-person visit. Study staff will collect your completed diary, and will take your temperature, blood pressure and heart rate. You will be asked about your health and any medicines you are taking. A blood sample of 15 mL (3 teaspoons) will be taken to test for antibody levels.

Visit 5 (phone call) Study Day 43 (5-10 minutes):
A member of the study staff will contact you to ask about your health and any medications that you are taking. We will also ask if you received any medical attention other than a routine visit.

Visit 6 (clinic visit) Study Day 60 (45-60 minutes):
You will be asked to return to the research clinic. Study staff will take your temperature, blood pressure, and heart rate. You will be asked about your health and any medicines you are taking. Study criteria will be reviewed, to make sure that you still qualify for the study. You will be asked to complete a brief assessment. You will receive the second dose of Shingrix® vaccine. You will need to stay in the clinic for at least 15 minutes after that to be watched for any reactions. You will be given a symptom diary form, a measurement tool and thermometer (if needed), and shown how to use them for this second vaccination.

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Visits 7 and 8 (phone calls) Study Day 69 and Study Day 103 (15-30 minutes):
A member of the study staff will contact you to review the information about your symptoms and medications that you should have been recording daily in the symptom diary. We will also ask if you received any medical attention other than a routine visit.

Unscheduled Visit: If you experience a severe reaction (as described in the "What are the Risks of the Study?" section below) after the vaccine(s), the study team may ask that you come for an additional research clinic visit. During this visit, the study team will take your vital signs (just like in Visit 1), and you will be asked about any changes in your health or medications you are taking.

HOW LONG WILL I BE IN THIS STUDY?

You will be in this study for approximately 3 1/2 months. 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.

Clinically relevant results will be communicated with you. When the study is complete, you will be informed which influenza vaccine you received. You will receive two copies of a letter stating which influenza vaccine you received, one for your records and one to give to your primary care provider. You will be responsible for informing your primary care provider about which vaccine you received. You will also receive a letter containing a summary of the study results when they are available.

WHAT ARE THE RISKS OF THE STUDY?

There may be some risks from being in the study. Risks associated with drawing blood from your arm include momentary discomfort and/or bruising. Infection, excess bleeding, clotting, or fainting are also possible, although unlikely. Staff will apply direct pressure to the blood draw site to reduce any bruising. Sterile techniques will be used to prevent infection at the site where blood will be drawn.

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With every medicine, including vaccines, there is a chance of side effects. There may also be risks, discomforts, drug interactions or side effects from these vaccines that are not yet known.

During this study, you will receive a Shingrix® vaccine and a flu vaccine (either FLUAD™ or Fluzone® High-Dose) that are approved by the FDA and recommended for use in the United States. The potential side effects from these study vaccines will not be different from what you would experience if you received these vaccines as part of your regular care. It is unknown if giving these two vaccines, potentially with novel adjuvants in both, at the same time will result in more or worse side effects.

Possible risks of receiving the Shingrix® vaccine include:

- pain,
- redness, or swelling where the shot was given,
- fever,
- chills or shivering,
- muscle aches,
- headache,
- fatigue,
- nausea,
- vomiting,
- diarrhea,
- abdominal pain

These reactions usually resolved in 2-3 days.

Possible risks with receiving the Flu vaccine include:

- redness,
- swelling,
- pain where the shot was given,
- fever,
- body aches,
- headache,

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- fatigue,
- nausea,
- cough,
- hoarseness,
- sore, red or itchy eyes,
- itching

These reactions usually resolved in 2-3 days.

Guillain-Barré syndrome (GBS) is a rare but serious condition that can occur after certain infections or after receiving certain vaccines such as the flu vaccine. There is a small increased risk of GBS (about 1or 2 additional cases per million people vaccinated) after vaccination with flu vaccine. The risk of GBS following Shingrix vaccination is 3 to 6 cases per million people vaccinated. GBS causes inflammation and damage to the nerves in your body. Minor symptoms such as muscle tiredness or more severe symptoms, such as paralysis (weakness, or inability to move certain parts of the body) may occur.

Very rarely, occurring in about 1 in every 1 million vaccine doses administered, there can be a serious allergic reaction to any vaccine. These reactions can cause skin rash (hives), difficulty breathing, swelling around the mouth, throat, or eyes, a fast pulse, sweating, or loss of blood pressure, and would happen within a few minutes to a few hours after the vaccination. If these reactions occur, they can usually be stopped by the study staff giving emergency medications. If you experience these reactions away from the study site, you should get immediate medical care and then contact the study doctor.

Some people get severe pain in the shoulder and have difficulty moving the arm where a shot was given. This happens very rarely. As with any vaccine or medication, there is a very small chance of a fatal reaction, although researchers do not expect this to occur.

For your safety, you must tell the study doctor or nurse about all the prescription drugs, over-the-counter (OTC) drugs, and supplements that you are taking before you start the study and before taking any of these products while you are on the study.

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There may be risks to you, discomforts, drug interactions or side effects that are not yet known. There may be other unknown risks to you that may be unforeseen. Study staff will update you in a timely way about any new information that may affect your decision to stay in the study.

If you have a severe or life-threatening reaction, you should call 911 or your doctor and seek immediate medical care.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

There may be direct medical benefit to you. Study participation will confirm that you receive the recommended Shingrix® and flu vaccinations. The Shingrix® vaccine has been shown to be effective in the prevention of herpes zoster (shingles) in older people. The two flu vaccines in this study have both been shown to prevent influenza in older people. You may develop protective antibodies against influenza. Information learned from this study may also help researchers understand the safety of administering two vaccines with adjuvants at the same time.

WHAT ALTERNATIVES ARE THERE TO PARTICIPATION IN THIS STUDY?

Shingrix®, FLUAD™ and Fluzone® High-Dose vaccines are available outside of this study. Please talk with the study team or your regular health care provider for more information.

WILL MY INFORMATION BE KEPT CONFIDENTIAL?

There is the potential risk of loss of confidentiality. Your personal health information will be collected as part of this study. Every effort will be made to keep your information confidential. Personal information, such as your name, and contact information will be kept in a separate secure location identified only by study subject number. The study records will be identified only by study subject number, and your name, initials or other personally identifiable information will not be used on study documents. Your name, initials, date of birth or other personal identifying information will not be used in publications or reports.

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.

Your records may be reviewed in order to meet federal or state regulations. Reviewers may include representatives from the Duke University Health System Institutional Review Board, as well as the CDC, and FDA. If any of these groups review your research record, they may also need to review your entire medical record.

The study results will be retained in your research record for at least six years after the study is completed. 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. 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.

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:

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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 subjects.

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 Food and Drug Administration (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 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.

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.

WHAT ARE THE COSTS TO YOU?

You will receive the Shingrix® vaccine and the flu vaccine at no cost. There are no additional costs to you associated with this study. However, routine medical care (services that you would have received whether or not you were in this study) will be charged to you or your insurance company.

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We will monitor your Duke Clinic charges to make sure that tests and studies done solely for research purposes are charged correctly. If you have any questions or concerns about appropriate billing, contact Dr. Schmader or the study team.

WHAT ABOUT COMPENSATION?

All study participants will be compensated $50 after completing each study visit and $25 after completing each phone call. Payments will be made via ClinCard and will be combined for efficient processing. Payments will be made for completed study visits.

If an unscheduled visit is needed to assess any adverse reactions to the vaccine(s), you will receive an additional $25 for completion of that visit.

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., your Duke physicians, or the Centers for Disease Control to provide monetary compensation or free medical care to you in the event of a study-related injury.

For questions about the study or research-related injury, contact Dr. Schmader at *919-660-7500* during regular business hours and at 919-477-1324 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.

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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. Schmader in writing and let him know that you are withdrawing from the study. His mailing address is: Dr. Kenneth Schmader, Duke Health-Division of Geriatrics, DUMC Box 3003, Durham, NC 27710. Once you withdraw consent, you can no longer take part in the study. You may also contact the study team to notify them of your decision to withdraw from the study by calling (919) 660-7581 during regular business hours. However, the study doctor may continue to use and share your health information that was collected before you stopped your consent.

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 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 changes in medical practice, or problems with the study. If this occurs, you will be notified and your study doctor will discuss other options with you.

CONSENT FOR STORAGE OF BLOOD AND FUTURE TESTING

Your blood samples will be stored at the Duke Human Vaccine Institute lab, and labeled only by a unique study subject number and will not be labeled with any identifying information such as your name or initials. Samples will be kept confidential to the best of our ability within state and federal law. After all antibody level tests are done, we would like to keep any remaining samples to use in possible future research studies. These studies may test for additional aspects of your immune response to the flu vaccine. No human genetic tests will be performed on your samples. Your stored samples will be linked to the information (including personally identifiable information) that you have provided to this study.

You will not receive results of any future testing that is done on these samples. Your decision regarding future research will not affect your participation in this study.

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If you agree to allow your blood to be kept for future research with identifying information that could link your sample to you, you are free to change your mind at any time. We ask that you contact Dr. Schmader in writing and let him know you are withdrawing your permission for your identifiable blood to be used for future research. His mailing address is: Dr. Kenneth Schmader, Duke Health-Division of Geriatrics, DUMC Box 3003, Durham, NC 27710. You may also choose to contact the study team at (919) 660-7581 to inform them of your decision to withdraw your permission for your blood to be used for future research. At that time, we will ask you to indicate in writing if you want the unused identifiable blood destroyed or if your samples (having all identifying information removed that would link the sample to you) could be used for other research.

PLEASE INITIAL your decision about permission for us to use your leftover samples for future research (indicate only ONE option):

_____**YES**, you may store my unused blood samples and use for future research.
_____**NO**, you may not use my unused blood samples for future research.

Your blood samples and/or data may be stored and shared for future research without additional informed consent if identifiable private information, such as your name and medical record number, are removed. If your identifying information is removed from your samples or data, we will no longer be able to identify and destroy them.

The use of your data and samples may result in commercial profit. You will not be compensated for the use of your data and samples other than what is described in this consent form.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?
For questions about the study or if you have problems, concerns or suggestions about the research, contact Dr. Schmader at 919-660-7500 during regular business hours and at 919-477-1324 after hours and on weekends and holidays. The Research Team can also be reached by calling 919-660-7581 during regular business hours.

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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 Duke University Health System Institutional Review Board (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