Project Title: Persistence Of Protection Conferred By Shingrix Against Herpes Zoster In Older Adults

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ICF Cohort 1-2

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Study Title: **Persistence of Protection Conferred By Shingrix Against Herpes Zoster In Older Adults**

Cohorts 1 & 2 – Zostavax or Shingrix ≥ 5 years ago

You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part. Taking part in this study is your decision and you may change your mind at any time. Your participation is voluntary.

Key Information Summary

What follows is a summary of the research study to help you decide whether or not to participate. Detailed information is provided after the key information.

The purpose of this research is to understand more about how the shingles vaccine, Shingrix, prevents shingles infection. Researchers do this by giving a dose of Zostavax to people who've had a shingles vaccine in the past. Zostavax is a shingles vaccine that has live chicken pox virus in it (which, in the vaccine, does *not* cause shingles). The body mounts a response to this virus to prevent infection. By drawing blood at 4 time points along the way, researcher learn more about how the vaccines prevent shingles.

Participation will last approximately one week.

- Four visits take place at Day 0, 1, 3, and 7.
- Study staff will ask you about your medical history and what medications you take.
- About 4 tablespoons of blood is drawn at every visit.
- You will be given the Zostavax injection on Day 0.
- Study staff will contact you at Day 9 to ask how you're feeling and if you've experienced any health changes. This contact will conclude your participation in the study.
- You will be paid $50 for each in-person visit you complete.

Risks include:

- Zostavax - Injection site reactions like redness, swelling, pain and tenderness. Very rarely, a brief, painless blistery rash limited to the site of injection may develop.
- Shingrix - These same injection site reactions as well as itching. General reactions such as tiredness, muscle pain, headache, chills, fever, and digestive symptoms like nausea, diarrhea or stomach ache may also occur
- Blood draws – may cause pain when the needle goes into your vein and you may experience bruising.
- Skin biopsy – potential for infection where the needles goes in. There is also a small chance that you could have an allergic reaction to the numbing medicine.

You will be given the option to receive the Shingrix vaccine, offered as a courtesy at the end of the study. Choosing to receive Shingrix is entirely optional and up to you and your physician. If you choose to receive Shingrix, you would return to the study site in about 2 months to receive the first dose of Shingrix, and again 2 months later to receive the 2nd and final dose. You will not be paid for these visits.

An alternative to participation is to not participate in the study and to obtain the Shingrix vaccine in the community.

Why is this study being done?

This study plans to learn more about how the Food and Drug Administration (FDA) approved shingles vaccine, **Shingrix** (SRX), successfully limits a common infection (shingles) in older people. This knowledge may be applicable to the general problem of improving the effectiveness of other vaccines for older people.

Shingles (also called Zoster or Herpes Zoster) is an infection that is caused by the same virus that causes chickenpox. After getting chickenpox during childhood, the virus remains in the body. Shingles occurs when the virus becomes active after many years, most commonly after 50 years of age, causing a painful rash, with pain potentially lingering for weeks or longer after the rash is gone. The chance of getting shingles increases with age.

Two vaccines are currently approved by the FDA to help prevent shingles. Zostavax is a live virus vaccine which has been available since 2006, and prevents shingles about 50% of the time. If a person develops shingles after having received Zostavax, they tend to have a much milder case. Zostavax protection has been shown to last about 5 years. Zostavax is less effective the older a person is when they receive it.

Shingrix, which was approved by the FDA late in 2017, is not a live virus vaccine, but has an additive in the vaccine to boost your immune response. It has been shown to be about 97% effective at preventing shingles regardless of a person's age and so far has been effective for at least 4 years after vaccination. Shingrix has been recommended for the prevention of shingles by the government committee (ACIP) which makes national recommendations for vaccines in the US.

Because Zostavax has live virus in it, giving a dose of Zostavax to people who have received both vaccines (Zostavax or Shingrix) in the past, will allow researchers to learn how your body works in preventing shingles and how any shingles vaccination helps protect you.

You are being asked to be in this research study because you received the shingles vaccine, Zostavax or Shingrix, 5 years or more ago.

Other people in this study
Up to 140 people from your area will participate in the study.

What happens if I join this study?
If you join the study, you will need to visit the research clinic 4-6 times. Your participation in the study may last up to 3½ months.

At **Visit 1**, after signing this consent document, a member of the study team will review your medical history, current medications, and the study entry criteria, to ensure you meet all of the requirements to take part in this research study. You will have your temperature taken. About 4 tablespoons of blood will be drawn to measure immune response by placing a needle into a vein of your arm. You will be given a dose of the shingles vaccine, Zostavax, into the skin of your upper arm.

A punch biopsy consists of taking a small sample of your skin. Participants will have a punch biopsy done at the injection site at Visit 2, 3, or 4. Some participants will a have the punch biopsy at Visit 1, but this will be done prior to vaccination and on the opposite arm. This will be done once only. Before we take the sample, we will give you some medicine to numb the area. Then we will press a hollow needle into your skin. When we take the needle out, it will remove a small circle of skin called a "plug". If you do not wish to participate in this procedure, you may not be able to participate in the research study.

At **Visit 2, 3, and 4**, you will have blood drawn, about 4 tablespoons at each visit, and possibly the punch biopsy. You will be asked about any health changes at each visit. If, 5 years ago, you received Shingrix vaccine, your participation in the study will end with a **follow-up phone call** a couple days after Visit 4.

If, however, 5 years ago you received Zostavax vaccine, you will be offered the Shingrix vaccine as a courtesy at the end of the study. Choosing to receive Shingrix is entirely optional and up to you and your physician. This would require 2 more visits: Shingrix is given in 2 doses so at **Visit 5**, 60 days or more after Visit 1, you will be given the first dose and return approximately 2 months later for the second dose at **Visit 6,** approximately 60 days after Visit 5. Prior to each vaccine dose being given, your medical history and current medications will be reviewed, you will have your temperature taken. You will not be paid for these 2 visits but will be given the vaccine at no charge.

Please indicate if you would like to receive the 2 doses of Shingrix vaccine (beginning at Visit 5) by initialing one of the following:

_____ I choose **to receive the Shingrix** vaccine at the end of the study. I understand that I can
Initial change my mind about this at any time.

_____ I choose **NOT to receive the Shingrix** vaccine at the end of the study. If I change my
Initial mind I understand that I must let study staff know prior to Visit 5.

Study Procedures

Cohorts 1 & 2 – Zostavax or Shingrix ≥ 5 years ago	**Visit 1** Day 0	**Visit 2** Day 1	**Visit 3** Day 3	**Visit 4** Day 7 (+3)	**Phone** +48 hours after V4	**Visit** Day 60 (+30)	**Visit 6** Day 120 (+ 30)
Informed consent, review of eligibility criteria	•						

Medical history and current medications	•					•[2]	•[2]
Blood draw	•	•	•	•			
Pre-vaccination body temperature	•					•[2]	•[2]
Vaccination – Zostavax dose	•						
Punch biopsy of Zostavax site[1]	•[1], *or*	•, *or*	•, *or*	•			
Vaccination – Dose 1 Shingrix[2]						•[2]	
Vaccination – Dose 2 Shingrix[2]							•[2]
Adverse event assessment	•	•	•	•	•		

[1]Punch biopsy done on Day 0 is on opposite arm, prior to vaccination

[2] If rec'd Zostavax 5 years previously and choose to receive Shingrix at study conclusion

What are the possible discomforts or risks?
Discomforts you may experience while in this study include the following.

Zostavax dose risks include injection site reactions such as local redness, swelling, pain and tenderness, itching, bruising, warmth, and possibly headache. Very rarely, a brief, painless blistery rash limited to the site of injection may develop.

Blood draw - In this study we will need to get a total of about 1 cup of blood from you. We will get blood by putting a needle into one of your veins and letting the blood flow into a glass tube. You may feel some pain when the needle goes into your vein. A day or two later, you may have a small bruise where the needle went under the skin.

Punch Biopsy -There are some risks to taking a sample of skin this way. There is a small chance that you could get an infection where the needles goes in. There is also a small chance that you could have an allergic reaction to the numbing medicine. After your skin heals up, you may have a small scar where we take the sample.

Shingrix – You will receive a handout called a Vaccine Information Sheet which will provide information about Shingrix.

The most frequent side effects occur at the injection site and include pain, redness, swelling, and itching. These side effects were usually mild, however occasional severe local reactions, mainly pain, were reported. These local reactions usually went away within 3 to 4 days. Other side effects that sometimes occurred included: tiredness, muscle pain, headache, chills, fever, and digestive symptoms (nausea, vomiting, diarrhea or stomach ache) and general unwellness (malaise). These symptoms were also usually mild and resolved within few days.

The Shingrix vaccine may cause some side effects that are not known at the present time. However, you will be notified immediately if during the course of the study any new findings (including findings from other studies or in animals) regarding any risks involved with the shingles study vaccine are discovered.

Risk of receiving multiple shingles vaccines - Shingrix is recommended for people who previously had Zostavax or prior shingles.

There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.

Certificate of Confidentiality

This study has been issued a Certificate of Confidentiality from the federal government to help protect your privacy. The Certificate prohibits the researchers from disclosing your name, or any identifiable information, document or biospecimen from the research, with the exceptions listed below. A certificate provides protections against disclosing research information in federal, state, or local civil, criminal, administrative, legislative or other proceedings.

These protections apply only to your research records. The protections do not apply to your medical records.

The researchers may disclose your name or identifiable information, document or biospecimen, under the following circumstances:

- To those connected with the research,
- If required by Federal, State or local laws,
- If necessary for your medical treatment, with your consent,
- For other scientific research conducted in compliance with Federal regulations,
- To comply with mandated reporting, such as a possible threat to harm yourself or others, reports of child abuse, and required communicable disease reporting, or
- Under other circumstances with your consent.

A Certificate of Confidentiality does not protect information you or a member of your family voluntarily release.

The study may include risks that are unknown at this time.

What are the possible benefits of the study?
This study is designed for the researcher to learn more about immune response to the Shingrix vaccine. This study is not designed to treat any illness or to improve your health. Also, there may be risks, as discussed in the section describing the discomforts or risks.

Who is paying for this study?
This research is being sponsored and payed for by the National Institutes of Health (NIH). Merck & Co. is providing Zostavax for the study.

Other information that needs to be disclosed
One of the study doctors, Dr. Myron Levin, has consulted for Merck Sharp & Dohme Corp., and shares, with the University of Colorado School of Medicine, a partial interest in a patent for Zostavax. In addition, Dr. Levin has consulted with GlaxoSmithKline Biologicals, the company that makes Shingrix. Dr. Adriana Weinberg is the spouse of Dr. Levin. Please feel free to ask any further questions you may have about this matter.

Will I be paid for being in the study?
You will be paid $50.00 for each in-person visit in this study that you complete, for a total of $200.00. If one of the visits includes the punch biopsy you will be paid an additional $50.00 for that visit. If you leave the study early, or if we have to take you out of the study, you will be paid only for the visits you have completed.

It is important to know that payments for participation in a study are taxable income.

Will I have to pay for anything?
It will not cost you anything to be in the study.

Is my participation voluntary?
Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

Can I be removed from this study?
The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason.

What happens if I am injured or hurt during the study?
If you have an injury while you are in this study, you should call *Adriana Weinberg, MD,* immediately. Her phone number is *303/724-4480.*

We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?
The researcher carrying out this study is Adriana Weinberg, MD. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Dr. Weinberg at 303/724-4480 or Dr. Myron Levin, MD at 303/724-2451. You will be given a copy of this form to keep.

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.

You may have questions about your rights as someone in this study. You can call Dr. Weinberg with questions. You can also call the responsible Institutional Review Board (COMIRB). You can call them at 303/724-1055.

Optional Consent for Data and Specimen Banking for Future Research
Dr. Weinberg would like to keep some of the data and blood that is taken during the study but is not used for other tests. If you agree, the data and samples will be kept and may be used in future research to learn more about improving vaccines for older people. The research that is done with your data and samples is not designed to specifically help you. It might help people who don't respond well to vaccines in the future. Reports about research done with your data and samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your data and samples will not affect your care.

The choice to let Dr. Weinberg keep the data and samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as part of the study. If you decide now that your data and samples can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want Dr. Weinberg to use your data and samples any longer, and they will no longer be used for research. Otherwise, they may be kept up to 5 years.

When your data and samples are given to other researchers in the future, Dr. Weinberg will not give them your name, address, phone number or any other traditionally identifying information that will let the researchers know who you are.

Your data and samples will only be used for research and will not be sold. The research done with your data and samples may help to develop new products in the future, but there is no plan for you to be paid.

The possible benefits of research from your data and samples include learning more about what causes shingles and other diseases, how to prevent them and how to treat them. Future testing *will not* look at large chunks of your DNA (whole exome testing) nor all of your DNA at once (whole genome testing). The greatest risk to you is the release of your private information. Dr. Weinberg will protect your records so that your name, address and phone number will be kept private. Information and specimens which are collected are shared coded, stripped of identifiers. Only Dr. Weinberg will have access to the code. The chance that this information will be given to someone else is very small. There will be no cost to you for any data or sample collection and storage by Dr. Weinberg.

Please read each sentence below and think about your choice. After reading each sentence, circle "yes" or "no." If you have questions, please talk to your doctor or nurse. Remember, no matter what you decide to do about the storage and future use of your data and samples, you may still take part in the study.

1. I give my permission for my data, blood, and/or tissue samples to be kept by Dr. Weinberg for use in future research to learn more about immune response to zoster viruses.

   _____YES _____NO _____Initials

2. I give my permission for my study doctor (or someone he or she chooses) to contact me in the future to ask me to take part in more research.

   _____YES _____NO _____Initials

3. I give my permission for my data, blood, and/or tissue samples to be used for research about other health problems (for example: causes of heart disease, osteoporosis, diabetes).

   _____YES _____NO _____Initials

I agree to take part in the study having to do with research on data, blood, and/or tissue samples as indicated above.

Signature_____Initials_____Date_____

Who will see my research information?
The University of Colorado Denver (UCD) and its affiliated hospital(s) have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institution involved in this study includes the University of Colorado Denver and University of Colorado Hospital.

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the UCD and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Dr. Adriana Weinberg, MD
MS 8604
12700 E. 19th Ave.
Aurora, CO 80045

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- People at the Colorado Multiple Institutional Review Board (COMIRB)
- The study doctor and the rest of the study team.
- The National Institutes of Health, the organization paying for this research study.
- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator.

Some of the research procedures involve genetic testing or the use of your genetic information. Your genetic information will not be released to others. This study *will not* look at large chunks of your DNA (whole exome testing) nor all of your DNA at once (whole genome testing).

The investigator (or staff acting on behalf of the investigator) will use your information for the research outlined in this consent form. They will also make *all or some* of the following health information about you collected in this study available to: Dr. David Koelle at the University of Washington.

Information about you that will be seen, collected, used and disclosed in this study:

- Name and Demographic Information (age, sex, ethnicity, address, phone number, etc.)
- Your social security number for payment only
- Research Visit and Research Test records
- Tissue samples and the data with the samples.

What happens to Data, Tissue, Blood and Specimens that are collected in this study?
Scientists at the University of Colorado Denver and the hospitals involved in this study work to find the causes and cures of disease. The data, tissue, blood and specimens collected from you during this study are important to this study and to future research. If you join this study:

- The data, tissue, blood, or other specimens given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data, tissue, blood, or other specimens collected from you.
- If data, tissue, blood, or other specimens are in a form that identifies you, UCD or the hospitals involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

HIPAA Authorization for Optional Additional Study Procedures
In this form, you were given the option to agree to additional, optional research procedures. You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional procedures, as described above.

If you decline to give us permission to use and disclose your information, you cannot take part in these optional procedures, but you can still participate in the main study. **Please initial** next to your choice:

_____I give permission for my information, from the optional procedures I have agreed to above, to be used and disclosed as described in this section.

_____I **do not** give permission for my information for any optional procedures to be used and disclosed; I understand that I will not participate in any optional procedures.

Agreement to be in this study and use my data
I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Signature:_____ Date:_____

Print Name:_____

Consent form explained by:_____Date:_____

Print Name: _____

Witness Signature:_____ Date_____

Witness Print Name:_____

Witness of Signature ☐

Witness of consent process ☐