VERBAL INTRODUCTION

You are being invited to take part in a research study testing whether a dietary supplement Lysulin can reduce the level of blood sugar and glycated hemoglobin. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive. Taking part in this study is completely voluntary.

Read the information below carefully and discuss it with family and friends if you wish. Ask one of the study staff if there is anything that is not clear or if you would like more details. Take your time to decide. If you do decide to take part in this study, your signature on this consent form will show that you received all the information below, and that you were able to discuss any questions and concerns you had with a member of the study team. If you are participating in any other research study, you must inform the study staff now.

Department of Veterans Affairs

Phoenix VA Health Care System (PVAHCS)
650 East Indian School Road
Phoenix, AZ 85012

Phoenix VA Health Care System Research Consent Form

Version Date:10/28/2019

Principal Investigator / Researcher: Juraj Koska, PhD

Title of Study: The Effect of Lysulin on Glycemic Control and Advanced Glycation in Inadequately Controlled Type 2 Diabetes Mellitus: A Double blinded Placebo Controlled Study (eRD 1185)

1. WHAT IS THIS STUDY ABOUT AND WHY ARE WE DOING IT?

You are being invited to take part in a research study about the effect of dietary supplement Lysulin on blood sugar and glycated hemoglobin. The Carl T. Hayden Medical Research Foundation is the sponsor of the study in collaboration with Lysulin, Inc.
Lysulin is an over the counter dietary supplement pill to be taken by mouth three times a day. It contains naturally present ingredients, including lysine – a part of normal body proteins, a zinc – a mineral that is part of many body structures, and vitamin C. Lysulin is used along with diet, exercise and diabetes medications to lower blood sugar levels in patients with diabetes (condition in which blood sugar is too high because the body does not produce or use insulin normally).

A. What is the purpose, procedures, and duration of this research study?

With this study we hope to learn if adding the nutritional supplement Lysulin to usual daily diabetes treatment compares to adding a placebo to usual diabetes treatment in lowering blood sugar. If you choose to take part in the study you will be asked to take 2 tablets, 3 times a day for 12 weeks of either the study supplement or a placebo. A placebo is a fake supplement without the nutritional supplement ingredients. Your participation in this study will include 3-4 visits to the clinical study site. At each visit you will have blood taken by a trained study team member and answer questions about your health and medical history. You may receive a telephone call during the study to ask how you're doing with the study drug. Your total time participating in the study will last about 3 months.

For a more complete description of study procedures, refer to Section 4 beginning on page 2.

B. What are the reasons I might choose to volunteer for this study?

You may or may not receive any benefit from being in this study If you take part in this study other people with Type 2 Diabetes may be helped. You may receive information from blood test that is done in this study, but these tests may not have any impact on your health.

C. What are the reasons I might choose not to volunteer for this study?

Reasons you may not choose to take part in this study are if you do not want your blood drawn. Lysulin may cause lowering of your blood sugar and you may experience symptoms of low blood sugar such as lightheadedness, anxiety and sweating.

You do not have to take part in this study to be treated for your Type 2 Diabetes. Other treatment for your diabetes is available. Your other choices may include getting the usual standard of care without being in the study or you may choose to volunteer for another study.

Participant's Name:

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Last **First** **Middle**

Last 4: _____

*Date of Birth:*_____

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You can discuss the risk and benefits of other treatment choices with your study team or health care provider.

D. Do I have to take part in this study?

Taking part in this study is completely voluntary. You can choose to participate or not. If you choose not to volunteer in this study, you will not lose any services, benefits, or rights you would normally have.

2. WHAT IS THE PURPOSE OF THIS STUDY?

- The study will test the effect of Lysulin on blood sugar and glycated hemoglobin levels.
- You are being asked to participate because you have diabetes with higher than recommended blood sugar levels on your current diabetes drugs.
- In some patients with diabetes, adequate blood sugar controls cannot be achieved even with very high-doses of current diabetes drugs. Further increase in doses may cause serious adverse events. It has been shown in some patients with diabetes that Lysulin may lower blood sugar when added to current diabetes medication without risk of adverse events
- The study will enroll up to 60 participants at the Phoenix VA

3. HOW LONG WILL I BE IN THIS STUDY?

This research study is expected to take approximately 6 months. Your individual participation in the project will take about 3 months.

4. WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

You will be asked to participate in 3-4 visits:

Screening visit

You will first be screened to find out if you qualify and are healthy enough to participate safely. If the screening process is too tiring to complete in one day, we may split the screening visit and do some of the tests a week or two later to make it easier for you. During the screening visit, we will look at your medical record and ask you for your medical history, what medication you take, and then give you a physical exam. The screening will include a blood test to find out how much sugar and fat is in your blood and to make sure your liver and kidneys are working properly. When you arrive, we will check your weight, height, blood pressure, and pulse. If, done as a single visit, the screening visit will take approximately 2 hours. All samples collected will be stored at the Phoenix VA.

Study Visit 1

You will be asked to return to the research department for visit 1 within about 1 week of the screening visit. Before this visit, you will be asked to eat your normal diet prior to your visit date. You will also be asked to come in the morning after an overnight fast for blood draws. We will check your weight, blood pressure, and pulse. More questions may be asked to ensure there are no reasons you cannot take part in the study. For the blood draw, you will be seated in the comfortable chair. We will collect about 3 tablespoons of blood. You will then be selected by a chance to Lysulin or placebo (a similarly looking pill that does not contain Lysulin) and given a package containing study pills (Lysulin or placebo). You will be given about 6 weeks' supply of Lysulin or placebo and asked to take 2 pills per mouth three times a day with main day meals. You will be asked to keep the study pills in a safe place for your use only and away from children

You will be asked not to change your diet or exercise routine while taking part in the study. We will call you after about one week to know how you are doing with taking the pills and if you have had any side effects from the study medication.

Study Visit 2
After 6 weeks from visit 1 you will be asked to come in around 8 am after an overnight fast for blood draws. We will also check your weight, blood pressure, and pulse, and ask if you have had any side effects from the study pills. Blood tests will be performed to make sure you are having no ill effects during the study. At this visit you will bring in your leftover study pills. Study pills will also be provided for an additional 6 weeks.

Study Visit 3
You will be asked to return 6 weeks after visit 2, you will be asked to come in around 8 am after an overnight fast for blood draws. We will also check your weight, blood pressure, and pulse, and ask you if you have had any side effects from the study medication or other adverse events. At this visit, you will bring in your leftover study pills. Blood tests will be performed to make sure you are having no ill effects during the study.

Additional Study Visits
There may be additional brief visits if you are having concerns regarding the pills or other study issues. These will be scheduled as needed. We will also contact you by phone between visits to make sure you are doing well and have no concerns regarding the medication or other study issues.

All study procedures will be overseen by study Co-Investigator Peter Reaven, MD. Blood draws and vital signs will be performed by certified Research Assistant.

Participant's Name:

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Last **First** **Middle**

Last 4: _____

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Keep your study appointments. If it you miss an appointment, please contact the investigator or research staff to reschedule as soon as you know you will miss the appointment.

Tell the investigator or research staff if you believe you might be pregnant or might have gotten your partner pregnant.

While participating in this research study, do not take part in any other research project without approval from the investigators. This is to protect you from possible injury from things such as extra blood drawing, extra X-rays, or potential drug interactions. Taking part in other research studies without first discussing it with the investigators of this study may invalidate the results of this study, as well as that of the other studies.

5. WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

Any procedure has possible risks and discomforts. The procedures in this study may cause all, some, or none of the risks or side effects listed. Rare, unknown, or unexpected risks also may occur.

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

Risks of the usual care you receive are not risks of this study. Those risks are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care.

- (1) Lysulin
  Lysulin may cause changes in your blood sugar. You should know the symptoms of low (e.g., sweating, anxiety, nervousness, tremor, difficulty thinking, excess sleepiness) and high blood sugar (e.g., fatigue, excess urination) and what to do if you have these symptoms.
  Some rare side effects can be serious. If you experience any of these symptoms, inform us and call your doctor immediately:
  - rash
  - hives
  - swelling of the face, lips, tongue or throat
  - difficulty breathing or swallowing
  - hoarseness

- (2) Blood drawing

There may be some discomfort, bruising, or bleeding at the site where the blood is drawn. Rarely, fainting occurs because of drawing blood.

- (3) Inclusion of Women of Childbearing Potential
  The safe use of Lysulin in pregnant women and nursing mothers has not been established. Consequently, there may be risks to you (or to your embryo or fetus) if you are or may become pregnant that are unknown. Women of childbearing potential enrolling in this study must (i) have been using a birth control measure (an intrauterine device (IUD), birth control pills, a condom, diaphragm, or abstinence) for the previous three months, (ii) must have a negative pregnancy test, and (iii) must agree to continue to use a birth control measure for the duration of the study. If, while participating in the study, you suspect you have become pregnant, please contact the study physician immediately. Women are considered to be of childbearing potential unless they have been surgically sterilized (for example tubal ligation or hysterectomy) or are post-menopausal, that is, no menstrual period for more than 6 months. Nursing mothers may not participate in this study.

6. WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

We do not know if you will get any benefits from taking part in this research study. However, possible benefits may include reduced blood sugar. However, the information we get from this study might help others with your conditions.

7. WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?

You do not have to take part in this study to be treated for your diabetes. Other treatments choices are available, such as getting the usual or standard of care for diabetes without being in this study. You may also choose to take part in another diabetes study.

Lysulin is available outside of this study over the counter without a prescription.

Discuss these and other options with your study team or your health care provider.

8. HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

Taking part in this study will involve collecting private information about you. This information will be protected in the following ways:

- Study files will be locked in filing cabinets
- Study data will be kept on VA-secured computers protected with passwords
- Only study team members will have access to this information

There are times when we might have to show your records to other people. For example, someone from the Office of Human Research Protections, the Government Accountability Office, the Office of the Inspector General, the VA Office of Research Oversight, the IRB, our local Research and Development Committee, and other study monitors may look at or copy portions of records that identify you.

Information about you will be combined with information from other people taking part in the study. We will write about the combined data we have gathered. Any talks or papers about this study will not identify you.

A more detailed description of how we will use and protect your private information will be provided to you in a separate document, known as a HIPAA Authorization.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

9. MEDICAL TREATMENT AND COMPENSATION FOR INJURY

Every reasonable safety measure will be used to protect your well-being. If you are injured as a result of taking part in this study, the VA will provide necessary medical treatment at no cost to you unless the injury was due to your not following the study procedures. You do not give up any of your legal rights and you do not release the VA from any liability by signing this form.

If you should have a medical concern or get hurt or sick as a result of taking part in this study, call 602-277-5551 extension 7063 during the day or, after hours, contact Phoenix VA Health Care System operator at (602) 277-5551 by pressing 0 or by staying on the line until they answer. You should inform the operator that you are in a research study and give the name of the Principal Investigator of this study.

For emergency care, you should call 911 or VA Emergency Department (602) 277-5551, ext. 7199. If any medical problems occur in connection with this study, the VA will provide emergency care. You can also contact your Primary Care Provider in case you have any additional medical problems or questions. Emergency and ongoing medical treatment will be provided as needed.

10. PERSONS TO CONTACT ABOUT THIS STUDY

In case there are study-related questions or medical concerns, I have been told I can call Dr. Koska or his associates during the day at (602) 277-5551, extensions 7685 or 7063 or 5817, after hours, contact Phoenix VA Health Care System operator at (602) 277-5551 by pressing 0 or by staying on the line until they

answer. I will inform the operator that I am in a research study and will give the name of the Principal Investigator of the study.

If you have any questions about the conduct of this study or about your rights as a participant in this study, you should contact the Research Service Champion, (602) 277-5551, extension 7783 or 6697. The Champion will follow-up and may further connect you, as appropriate, with the Chairperson of the Institutional Review Board (IRB), the Chairperson of the Research and Development Committee, the Research Administrative Officer, or the Research Compliance Officer.

11. PARTICIPATION IS VOLUNTARY

It is up to you to decide whether or not to take part in this study. If you decide to take part you may still withdraw at any time. To withdraw your consent to participate, you need to inform the study team. Once you have withdrawn your consent, no further study visits are required. If you do not wish to be in this study or leave the study early, you will not lose any benefits to which you are entitled. If you don't take part, you can still receive all usual care that is available to you. Your decision not to take part will not affect the relationship you have with your doctor or other staff, and it will not affect the usual care that you receive as a patient. The specimen and study data collected on you prior to when you decided to stop being in the study will remain. No further information will be collected without your informed consent.

12. RIGHT OF INVESTIGATOR TO TERMINATE YOUR PARTICIPATION

Your participation may be terminated without consent if you (1) have developed a condition that might increase your risk for problems from any of the study testing, (2) are unable to take required amount of study pills or (3) if despite due diligence, laboratory technicians are unable to obtain adequate quantities of blood to be useful for further investigation.

The HIPAA Authorization which permits VA to use and release your medical record is a separate form that, unlike this consent form, must be revoked in writing. To ensure that VA cannot be forced to access your health records for this study after you withdraw your consent, you should also revoke your HIPAA Authorization. The study team can provide a HIPAA revocation form for you to use, or you can send a written statement that you revoke your HIPAA authorization to the revocation address on the study's HIPAA Authorization form.

13. WHAT IS THE COST TO ME AND PAYMENT FOR ME IF I TAKE PART IN THIS STUDY?

A. Costs to Participants:

You will not be charged for any treatments or procedures that are part of this study. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for VA care and medications that are not part of this study.

B. Payment Offered for Participation:

For your participation, you will be reimbursed $15 for screening visit and $25.00 per each study visit, up to a total of $90.00 for completing the entire study.

The reimbursement will be on a ClinCard, which works like a gift/credit card. When visits are completed, funds will be loaded onto your card. You will be able to use the funds within 1-2 hours. If you have issues when using this ClinCard, please contact the study team. The provider of the ClinCard (Greenphire) will not have access to your name or contact information. Instead, they will have your study ID number that will be provided to you by the study coordinator. If your ClinCard is lost or stolen, Greenphire cannot cancel your card if is lost or stolen, and the entire current balance on the card may be lost. However, you will be issued a new card for future payments. If you get more than $600 in one year from ClinCard, this will generate Internal Revenue Service (IRS) form 1099. Your SSN will be used for this purpose.

14. WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

Sometimes during the course of a research study, new information becomes available about the Lysulin that might change a person's decision to stay in the study. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from the study, your research doctor will arrange for your medical care to continue. If you decide to continue in the study, you might be asked to sign an updated informed consent form. Your research doctor could also decide to withdraw you from the study in your best interests. If so, he or she will explain the reasons and arrange for your usual medical care to continue.

Generally, tests done for research purposes are not meant to provide information for clinical treatment. Your individual results for this study will generally not be provided to you. There is a slight possibility that during this study, an investigator could discover something that could affect the health of you or your family. If this occurs, the finding will be reviewed by Dr. Peter Reaven to determine if it is in your best interest to contact you. If so, your primary/clinical care provider will contact you using the information you provided and will present possible risks or benefits of receiving the information. At that time, you can choose to receive or refuse to receive the result or finding.

15. WHO COULD PROFIT FROM THE STUDY RESULTS?

The use of your donated sample may be used for research that may result in scientific discoveries that may lead to new products, tests, or treatments. These discoveries may have potential commercial value. If this occurs, there are no plans to provide financial payment or benefits to you or your relatives.

Participant's Name:

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Last **First** **Middle**

Last 4: _____

*Date of Birth:*_____

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16. HOW WILL MY DATA AND / OR SAMPLES BE USED IN THE FUTURE?

Identifiable information, such as your name or date of birth, will be removed from the information and/or samples collected in this study. After removal, the information and/or samples may be used for future research or shared with other researchers without your additional informed consent.

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

The Principal Investigator Dr. Juraj Koska or a research team member has explained the study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other alternatives available to you. You have been given the chance to ask questions and obtain answers. You will receive a copy of this consent.

By signing this document below, you voluntarily consent to participate in this study. You also confirm that you have read this consent, or it has been read to you. A copy of this signed consent will also be put in your medical record.

I agree to participate in this research study as has been explained in this document.		
_____ Participant's Name	_____ Participant's Signature	_____ Date
_____ Name of person obtaining consent	_____ Signature of person obtaining consent	_____ Date

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