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UNIVERSITY OF PENNSYLVANIA COMBINED RESEARCH SUBJECT HIPAA AUTHORIZATION AND INFORMED CONSENT FORM

Protocol Title: Adrenergic Contribution to Glucose Counterregulation in Islet Transplantion

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Why am I being asked to volunteer?

You are being invited to participate in a research study because **you have type 1 diabetes and you have received islet cells transplanted in your liver.** Your participation is voluntary which means you can choose whether or not you want to participate. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also decide to discuss it with your family, friends, or family doctor. You may find some of the medical language difficult to understand. Please ask the principal investigator and/or the research team about this form. If you decide to participate, you will be asked to sign this form. Your doctor may be the principal investigator in this research study. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of this study. Before entering this study or at any time during the research, you may want to ask for a second opinion about your care from another doctor who is not an investigator in this study. You do not have to participate in any research study offered by your doctor.

IRB Approved from: 12-Oct-2020 to 11-Oct-2021

What is the purpose of this research study?

We are inviting you to participate in this research because you have type 1 diabetes and have received an islet cell transplant in your liver. As you know, islets from one or more organ donors' pancreas have been removed and transplanted into you. For this study, these islets that were transplanted into your liver to make and release insulin must still be functioning.

The purpose of this study is to test how your bodies' nerves and hormones affect these islet cells and their response to low blood sugar (glucose). This study will provide important information about how the islets in your liver (intra hepatic) protect you from low blood glucose.

We plan to identify whether it is nerves or hormones that help your transplanted islets respond to low blood glucose by having you undergo up to 3 separate hyperinsulinemic euglycemic-hypoglycemic clamps. This is similar to the metabolic tests you did when you were participating in your islet transplant study. The main difference is that during these tests you will receive an infusion of phentolamine, propranolol, or placebo. These infusions will help us determine if it is nerves or hormones that help protect you from low blood glucose. Both Phentolamine and Propranolol are FDA approved drugs for the lowering of blood pressure and heart rate; but in this study we are using these drugs in an investigational manner. In other words, we are trying to see if infusing them in your IV will allow us to gain new information on how your nerves and hormones affect the way your transplanted islets regulate your blood glucose.

Phentolamine is an α-adrenergic blocker (alpha blocker). Alpha blockers treat conditions such as high blood pressure and enlarged prostate glands. Alpha blockers relax certain muscles and help small blood vessels remain open.

Propranolol is a β-adrenergic blocker (beta blocker). Beta blockers are medications that reduce your blood pressure and heart rate. Beta blockers work by blocking the effects of the hormone epinephrine, also known as adrenaline.

In this study we are infusing Phentolamine and Propranolol because we are trying to see if these drugs create a condition which helps us understand the relationship your nerves and hormones have on your blood glucoses.

How long will I be in the study? How many other people will be in the study?

If you agree to participate in this research, your participation will last up to three months and will include 1 screening visit and up to 3 separate overnight visits for which the next day (study day) will consist of one of the above mentioned hyperinsulinemic euglycemic-hypoglycemic clamp.

If you have a history of cardiovascular disease you will not receive the phentolamine condition and if you have asthma you will not receive the propranolol condition.

The University of Pennsylvania is the only site performing this research. At UPenn we expect to screen approximately 15 adults in order to enroll a minimum of 12 adults in the study.

What am I being asked to do?

In this study you will have 1 screening visit and up to 3 overnight hyperinsulinemic clamp visits. During each Hyperinsulinemic clamp test we will be using one of 3 infusion interventions. Each of these 3 interventions will be infused via an IV bag beginning 30 minutes before the clamp starts. The infusion drip will last for 180 minutes at a very low level. The infusions you will receive are Phentolamine, Propranolol and Placebo in a random order. The order will be determined by the pharmacist and will not be known to you or to the study team.

You will be invited to spend the night in the Center for Human Phenomic Science the night before the test. The nurses will check you in, bring you dinner and make sure you are comfortable throughout the night. You will sleep with two IVs; one in each of your arms so the nurses may check your blood glucose and titrate your insulin (if needed) as you sleep. The morning of the test (at around 6:30am) an additional single IV will be placed. Two of the inserted IVs will be used for infusions and the third IV for blood draws.

Doing this hyperinsulinemic clamp involves infusing the following:
• insulin at a steady rate (based on your weight)
• glucose (dextrose) at varying rates --- the MD and/or NP calculate the rates based on your blood glucose reading measured every 5 minutes
• glucose stable isotope tracer (widely used glucose infusion especially prepared for research that traces how your body disposes of glucose during the test)
• intervention drug (phentolamine, propranolol or placebo).

To take part in this study you will need to:
1. Have been diagnosed with type 1 diabetes and have working islet cells that have been transplanted in your liver.
2. Be at least 21 years old and not yet 66 years old.
3. Meet certain criteria for your weight, insulin dosage and results of certain lab tests.
4. Use standard immunosuppression and are willing to follow all protocol procedures.

There are some exclusion criteria that may prevent you from being part of the study. These include certain medications and medical conditions. Your study doctor will be reviewing this to determine if any of the exclusions apply to you.

If you are female and of child-bearing potential and not currently nursing a baby, you will need to agree to use a highly effective method of birth control during your participation in the study. (See pages 6 & 7 of this consent form) Your study doctor or nurse will discuss with you birth control methods that are considered highly effective. If you are a female who can become pregnant, we will do a urine test to be sure you are not pregnant prior to beginning any testing at each of your visits.

All of the study day visits will be held in the UPenn outpatient Center for Human Phenomic Science (CHPS) located in the Perelman Center on 4 West. When you check-in for your overnight you will arrive to the inpatient CHPS located in the Dulles building #160 of the Hospital of the University of Pennsylvania. The nurses will take you to the Perelman Center in the early morning.
As with any overnight hospital stay, upon departure you will be given standard nursing departure instructions which will include a contact name and telephone number.

Additionally, within 24 hours of your departure from CHPS, the team nurse practitioner will call you to follow-up on how you are feeling.

The study visits are described in detail in the sections below.

Visit 0 (Screening)

The first visit is a screening visit to be sure that you are eligible for the study.

At the screening visit the following events will take place:
- A complete medical history and physical exam (height, weight, blood pressure etc.).

- We will ask you questions about your health, including any medical conditions you have and medications you take, insulin dosages and any other information that is needed to determine if you are eligible for the study.
- Several blood tests to test your organ function and your body's ability to make insulin.
- If you are female, a blood or urine pregnancy test.
- An electrocardiogram (ECG) (a test that checks the electrical activity of your heart).
- Complete a questionnaire about hypoglycemia (helps us calculate a Clark Score which identifies your level of hypoglycemia awareness) and complete a Hypoglycemia Awareness which identifies how severe your hypoglycemia is.
- A download and review of your personal glucometer
- Insertion of a continuous glucose monitor. (See description below. It is a sensor placed just under the skin that measures your tissue glucose levels for up to 7 days).

Continuous Glucose Monitor (CGM)

At the end of the screening visit, you will have a continuous glucose monitor (CGM) placed on your belly and you will wear it for up to a week. The CGM is a small continuous glucose sensor (about the size of a quarter) that will be attached with a tiny needle under your skin and will be worn home and remain in place for 7 days. The CGM will be inserted by a member of the study team who will instruct you on how to care for it at home. Wearing this monitor will help define your body's glucose patterns.

The CGM that you will be provided with is called iPro®2 Professional Continuous Glucose Monitor. This device is approved by the Food and Drug Administration (FDA).

The CGM kit has a sensor and a transmitter. The sensor has a plastic body and contains a thin, small needle and sensor wire about the size of a human hair. The sensor will be placed under the skin on your belly. Once inserted, the needle is removed and the sensor wire remains. The transmitter is about the size of a thumbprint and snaps on top of the sensor. Special tape is used to keep the sensor in place. The sensor wire continuously measures the glucose level in the fluid beneath the skin every 5 minutes. The glucose information is stored by the transmitter using radio waves. Once you return the transmitter to us we can retrieve your continuous glucose readings by sitting the transmitter in a docking station that is connected to a computer with a USB cord.

During the time you are using the CGM (7 days), you will need to check your blood sugar at least 3 times per day with your home blood glucose meter. We will provide you with instructions about when to check. If you do not have enough test strips for your own glucose meter we may provide you with a study glucose meter and enough test strips to cover the 7 days.

You may be asked to wear the CGM for an additional 7 days to collect additional glucose readings if we were unable to retrieve enough readings.

Following is a chart and description of the visits for your group:

GROUP 1 - TYPE 1 DIABETICS WITH INTRA-HEPATIC ISLETS

	Screening	***Overnight***	***Overnight***	***Overnight***
	Visit 1	**Visit 2**	**Visit 3**	**Visit 4**
Informed Consent	X			
[1] History and Physical Exam	X			

Glucometer (download / review)	X	X	X	X
ECG	X			
Hypoglycemia Questionnaires	X			
Blood Tests (HbA1c, CBC, Liver /Kidney Function, Glucose, C-peptide, TSH & Electrolytes)	X			
[2] Pregnancy Test	X	X	X	X
[3] 7-day CGMS	X			
[4] Euglycemic-Hypoglycemic Clamp (intervention random assignment)		X	X	X

[1] May be repeated at next visit if it is done later than 30 days
[2] If female
[3] May also be placed at any of the subsequent visits if unable to place at visit 1 for logistical reasons
[4] The interval between visits in group 1 will be between 1 and 4 weeks. The screening visit and first clamp may be done on consecutive days.
[5] Some participants will not attend a visit 4. Participants with coronary artery disease will not receive the phentolamine condition during the Euglycemic-Hypoglycemic clamp, and participants with asthma will not receive the propranolol condition during the Euglycemic-Hypoglycemic clamp,

After reviewing the results of the visit explained above, your research doctor will determine if you are eligible to participate in the studies. If you do not meet the eligibility criteria, your research doctor or study coordinator will discuss the reasons with you. If your research doctor determines you are eligible to participate, you will be randomized and scheduled for your additional 2 or 3 visits.

What is Randomization?

We will randomly assign an intervention to be used at each of your 2 or 3 clamp visits, meaning there is no predictable choice as to which of the 2 or 3 interventions will be done first. (...like the toss of a coin). You and the study team will not know which intervention you have received; which is in research is called "double blind". The 3 interventions are: phentolamine, propranolol or placebo. They are explained in the Risks section on page 5.

Overnight Visits 2, 3 & 4:

The interval between visits in group 1 will be between 1 and 4 weeks but not longer than 8 weeks. The screening visit and first clamp may be done on consecutive days. At each of these visits you will check into the research unit at the Hospital of the University of Pennsylvania the evening before the test between 4 and 7pm. You will be served dinner and the nurses will ask you to fast after 8pm. You will sleep with two IVs; one in each of your arms so the nurses may check your blood glucose and titrate your insulin (if needed) as you sleep.

The next day the following will occur:

- We will take your vital signs (blood pressure, heart rate, and breathing) and perform a b brief physical exam.
- We will ask you about any problems you have experienced and any unusual or unpleasant feelings you may have had since your last visit. (AE / SAE review).
- If you are female and could become pregnant, a urine or blood pregnancy test will be done.
- We will download and review your glucometer.
- We will perform the Hyperinsulinemic clamp test using one of the 3 interventions (see intervention details on bottom of page 5 & top of page 6). One of these 3 interventions will be

infused via an IV bag beginning 30 minutes before the clamp starts. The infusion drip will last for 90 minutes at a very low level. After spending one night in the CHPS (research unit) at the Hospital of the University of Pennsylvania, you will have a third IV placed. During the test the IV in one arm will be used for continuous blood sample access and the two IVs placed in the other arm will be used for the infusion of insulin, glucose, and a chemically modified glucose called a stable isotope. After 2 hours of receiving the stable isotope, insulin will be infused at a given rate while glucose will be infused at a varying rate. The two parts to this Hyperinsulinemic clamp and they are explained next.

Euglycemic part
In the initial euglycemic portion of this clamp test we will keep your blood glucose level at 90 mg/dl over a 2 hour period. Your blood glucose level will be checked every 5 minutes to confirm the levels and additional blood samples will be drawn to check how a variety of hormones respond to having a normal blood sugar and how your body responds in making glucose.

Hypoglycemic part
In the end hypoglycemic portion of this clamp test, we will gradually lower your blood glucose level to 50 mg/dl over a 2-hour period. Your blood glucose level will be checked every 5 minutes to make sure it is safe, and like above, additional blood samples will be drawn to check how a variety of hormones respond to your having a low blood sugar and how your body responds in making glucose.
During the test we will be monitoring your blood pressure and your heart. The entire test will take approximately 7 hours to complete, and ~ ½ cup total blood will be drawn

Following are specific details for the timing of the rates of infusion that will take place during the test:
• Glucose stable isotope Tracer starts 2 hours before the clamp start and will continue until the end of the clamp.
• Glucose (20% dextrose solution) Starts at ~9:00a.m and will be infused at a variable rate throughout the test until your blood glucose returns to normal after testing
• Drug (or placebo) infusion starts 30 minutes before the clamp start and will continue until the end of the clamp.
• Insulin infusion starts at the beginning of the clamp and will continue at a steady rate until the end of the clamp.

You will be given lunch after the test is over.

What are the possible risks or discomforts?

There are known possible risks and discomforts associated with most studies. As with any medication or testing procedure; there is a risk that a rare or previously unknown side effect, drug interaction, or allergy can occur. These unknown risks may affect you during your participation in the research and/or at some point in the future.

During each of the clamp tests you will wear a continuous heart rate monitor connected to a clinical monitoring unit (telemetry). Your heart rate and blood pressure will be recorded at least every 15 minutes.

Both Phentolamine and Propranolol are FDA approved for the lowering of blood pressure and heart rate; but in this study are being used in an investigational manner. In other words, we are trying to see if infusing them in your IV will allow us to gain new information on how your nerves and hormones

affect the way your transplanted islets regulate your blood glucose. These drugs infused through your IV during the clamp tests will help us determine if it is nerves or hormones that help protect you from low blood sugar.

Phentolamine
Phentolamine is an α-adrenergic blocker (alpha blocker). Alpha blockers treat conditions such as high blood pressure and enlarged prostate glands. Alpha blockers relax certain muscles and help small blood vessels remain open. Phentolamine may be associated with an increase in heart rate, a reduction in blood pressure, or both. It may also prompt orthostatic hypotension, a condition in which your blood pressure falls significantly when you stand up quickly. Rarely, myocardial infarction (heart attack) and cerebrovascular accidents (strokes) have been reported to occur in association with significant low blood pressure episodes. If you have a history of heart attack or stroke, you will not receive this condition.

Propranolol
Propranolol is a β-adrenergic blocker (beta blocker). Beta blockers are medications that reduce your blood pressure and heart rate. Beta blockers work by blocking the effects of the hormone epinephrine, also known as adrenaline. When you take beta blockers, your heart beats more slowly and with less force, thereby reducing blood pressure. Propranolol may be associated with both a decrease in heart rate, and/or a reduction in blood pressure. As with phentolamine, it may also prompt orthostatic hypotension. Propranolol has also been associated with bronchospasm (sudden contraction of the muscles in the passage-ways by which air passes to your lungs) If you have bronchial asthma you will not receive this condition. Please let your doctor know if you have any kind of upper respiratory infection (cold, flu, chest congestion) as your test will need to be re-scheduled.

Placebo
Placebo is a medical term for fake treatment. This term is used in research to describe an "inactive substance". We do this to be able to use the results from your placebo test and compare them to the results from your other two tests to see how blocking the nerve and hormone signals to your islets affects their response to low blood glucose. The placebo substance you receive in this study is saline solution. There is no additional risk associated with the administration of the IV saline infusion.

Risks from the Blood Draw:
The risks of having blood drawn include temporary discomfort or pain, bruising at the site of puncture, fainting, and infection or a small blood clot or swelling to the vein and area surrounding where the blood is drawn. Also, when a large amount of blood is taken, your iron levels may become low. These conditions may cause you to feel tired or weak. If that happens, other medications may be required to help reduce these side effects.

It is important for you to know that the amount of blood that will be drawn for research purposes during your screening visit and 3 clamps will not exceed 450mLs (almost 2 cups) in a 6 week period.

IV Risks
The risks of having IVs placed include discomfort, bruising, infection, fainting, blood clots, or infiltration of the IV solution, which could cause skin burning or tissue damage. However, these risks are very small and will be minimized by having experienced nurses and doctors continuously monitor the IV sites during the studies.

Risks from the Hyperinsulinemic Clamps:
The second part of the clamp study is designed to lower your blood glucose level to 50 mg/dl. You may feel lightheaded, dizzy, nauseous, sweaty, jittery, tired, or experience blurred vision from having

your blood glucose changed. There is a small risk that your blood glucose becomes extremely low for a prolonged period. If this happens, it could cause a seizure. To minimize this risk, blood glucose will be monitored throughout the test. We will rapidly correct any lower than expected blood glucose by giving you glucose through your IV or by mouth to return blood glucose levels to normal.

Risks from the Stable Glucose Isotope:

During the clamp test you will be given a stable glucose isotope through an IV. These substances are normally present in low amounts in food and in the environment. The isotopes are germ-free solutions mixed especially for research. There is a very small risk that giving you this solution may cause you to have an infection or fever. This risk is reduced by special testing of the isotopes prior to giving them in the IV.

Risks from the Continuous Glucose Monitor (CGM):

You may feel skin irritation at the site where the needle is placed. You may also have one or more of the following: bruising, discomfort, pain, bleeding, redness, raised bumps, local infection, and appearance of a small "freckle-like" dot where the needle was inserted. You may get an infection where the sensor was inserted. If there is pain, redness, irritation, or rash at insertion site, the sensor will be removed and re-inserted in a different site. Any infection, or sign of infection, will be treated immediately.

Reproductive risks:

You cannot participate in this study if you are currently pregnant or become pregnant at any time during the study. It is possible that effects from the study procedures could cause harm to unborn children or children who are breast-feeding. These effects could also harm the mother. It is also possible that harmful side effects that are not yet known could happen to both the mother and unborn or breast-feeding child.

If you are currently pregnant, it is important that you inform the investigator because you will not be able participate in the study. If you are able to become pregnant, you will be given a urine pregnancy test before entry into the study and at each clamp visit.

If you are sexually active, you must use medically accepted methods of birth control while you are on this study. Birth control methods which may be considered as highly effective include:

- Combined hormonal contraception associated with inhibition of ovulation (oral, intravaginal, transdermal)
- Progestogen-only hormonal contraception associated with inhibition of ovulation (oral, injectable, implantable)
- Barrier method of birth control to include: the diaphragm, cervical cap, male condom, or female condom/sheath plus spermicidal foam, sponges, or film
- Intrauterine device (IUD)
- Intrauterine hormone-releasing system (IUS)
- Bilateral tubal occlusion
- Vasectomised partner
- Sexual abstinence

If you should become pregnant while participating in this study, or if you suspect that you have become pregnant, you must contact the Principal Investigator Dr. Michael Rickels immediately and consult an obstetrician or maternal-fetal specialist. It is important that you inform the study doctor or study coordinators because you will not be able to continue to participate in the study.

Privacy Risks

There is the unlikely chance that your information is viewed by someone outside the research team who is not authorized to see your health information. However, we make special efforts to make sure that this does not happen.

Unknown Other Risks
There also may be side effects or risks that are not known at this time. If we become aware of any new risks, you will be told about them. You will be able to decide if you want to continue participation in this study.

Risks related to your normal medical care are not listed in this form. We encourage you to discuss these with your study doctor, your primary care provider, or another health care professional

What if new information becomes available about the study?
During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?
The results of this study may help you and other people with type 1 diabetes in the future.

You are not expected to get any direct benefit from being in this research study. Although you may not benefit directly from being part of the study, we will provide you with a summary of your CGM data as well as your lab results from the study. You and your doctor will be able to review this information after you have completed the study. This information may be helpful for making changes that could help your diabetes and / or islet transplant management.

You are not expected to get any benefit from being in this research study.

What other choices do I have if I do not participate?
Your alternative is not to participate in this study. Participation in this study is your choice. By participating in this study you are not receiving any treatment for your condition.

Will I be paid for being in this study?
When you complete this study, you will be compensated for your time. For each of the 3 visits where a clamp is completed you will receive $150.00. You will also receive $50.00 for the completion of the screening visit. The total amount you will receive for participation in this study is $500.00

Your compensation for this study will be made via a check from the University of Pennsylvania. Processing can take anywhere from 4 to 6 weeks. Please note: In order to be compensated for your participation in this study, you must provide your Social Security Number. The University of Pennsylvania is required to report to the IRS any cumulative payments for participation in research studies that exceed a total of $600 in a calendar year.

If you do not complete the study, you will be compensated for the number of visits you have completed. If you have questions about your compensation for taking part in the study, please contact Eileen or Amy at the telephone number listed on page 1 of this consent document.

Travel reimbursement
Should your participation in this study require long-distance travel involving air or rail; economy or coach-fare tickets will be reimbursed via a check from the University of Pennsylvania.

If your travel is short-distance; you will receive $11.00 in cash at each visit to cover your parking or your regional rail ticket expense.

Will I have to pay for anything?

The study will pay for the costs of the study office visits and all research supplies and procedures that are being used or done specifically for the study. This includes the CGM and blood glucose meter and test strips to be used while you wear the CGM for the 7 days.

The expense of your diabetic supplies and insulin will be your or your insurance company's responsibility. You will be using your own blood glucose monitor in this study and test strips will be your responsibility (except during the 7-days of CGM use).

You and your health insurance may be billed for the costs of medical care (any deductibles or applicable co-pays for routine office visits, scans and blood work) during this study if these expenses would have happened even if you were not in the study. An example of these routine costs billed to insurance would be some screening labs such as an HbA1c or liver/ kidney function tests.

Co-pays and deductibles are highly variable depending on your type of insurance so please talk to your study team if you need help in determining exactly what the amount of your payment would be if it was required.

What happens if I am injured from being in the study?

If you are injured in this study we will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, please tell Dr. Rickels who is in charge of the research study as soon as possible. Dr. Rickels' phone number is listed on the front page of this consent form.

When is the Study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed all visits, and all information has been collected. Your participation in this study may be stopped at any time by your physician, the Principal Investigator, or the University of Pennsylvania Institutional Review Board (IRB) or the Food and Drug Administration (FDA) without your consent because:

- Your physician or the Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The Principal Investigator or the University of Pennsylvania Institutional Review Board (IRB), or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at any time. Withdrawal will not interfere with your future care.

Who, outside the School of Medicine, might receive my information? How will my personal information be protected?

Results of laboratory tests and clinical procedures will be placed in your medical record and may be accessible to employees of the health system that are not part of the research team. This information may also be viewed by your insurance company during routine audits.

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. If this study is audited by The Office of Clinical Research they may review your research records. The study data and safety monitoring board (DSMB) may also review your records.

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.

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

Who may use and share information about me?

The following individuals may use or disclose your personal health information for this research study:

- The Principal Investigator and the investigator's study team
- Authorized members of the workforce of the UPHS and the School of Medicine, and University of Pennsylvania support offices, who may need to access your information in the performance of their duties (for example: for research oversight and monitoring, to provide treatment, to manage accounting or billing matters, etc.).

How long may the School of Medicine use or disclose my personal health information?

Your authorization for use of your personal health information for this specific study does not expire. Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Electronic Medical Records and Research Results

What is an Electronic Medical Record?

An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient) and are participating in a University of Pennsylvania research study, results of research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

If you have never received care within UPHS and are participating in a University of Pennsylvania research study that uses UPHS services, an EMR will be created for you for the purpose of maintaining any results of procedures performed as part of this research study. The creation of this EMR is required for your participation in this study. In order to create your EMR, the study team will need to obtain basic information about you that would be similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have). Results of research procedures performed as part of your participation in the study (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in this EMR.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g. health insurance company, disability provider, etc).

What information about me may be collected, used or shared with others?

The following personal health information will be collected, used for research, and may be disclosed during your involvement with this research study:

• Name, address, telephone number, email address, date of birth, social security number • Demographic information (e.g., age, sex, race/ ethnicity) • Socioeconomic information (e.g., education, number in household income, employment status) • Psychosocial and quality of life information • Medical conditions including complications of T1D, surgeries, and pregnancies • Medications • Family history • Laboratory Test Results	• Physical examination findings (e.g., blood pressure reading, heart rate, breathing rate and temperature, weight/BMI) • Information related to the onset & diagnosis of T1D • Treatment/management of T1D • Problems encountered in self-management of T1D • Results of tests, procedures and medical conditions you have had during your history of diabetes • Participation in other studies

Why is my information being used?

Your information is important so the research team may contact you during the study. Your personal health information and results of tests and procedures are being collected as part of this research study. It is necessary in order to do the research, oversee the research and to see if the research was done right. In some situations, your personal health information might be used to help guide your medical treatment.

Can I change my mind about giving permission for use of my information?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

You will be given a copy of this Research Subject combined Consent and HIPAA Authorization document describing your consent confidentiality and privacy rights for this study.

By signing this document you are not only agreeing to participate in this research study but also permitting the School of Medicine to use and disclose personal health information collected about you for research purposes as described above.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

You will be given a signed copy of this Research Subject combined Consent and HIPAA Authorization Form describing your confidentiality and privacy rights for this study.

Name of Subject (Please Print)	Signature of Subject	Date

I certify that to the best of my knowledge the participant understands the nature, demands, risks, and benefits involved in his/her participation in this study.

Name of Person Obtaining Consent (Please Print)	Signature	Date

Future Research Participation

In the future, our team or other investigators at Penn may wish to contact you regarding new studies that you may be eligible to participate in. Do you want to be contacted regarding research participation in the future? (Regardless of your choice, you may still participate in the study and your future care will not be affected in any way).

☐ ***Yes**, I give permission to be contacted regarding future research participation* _____ ***Initials***

☐ ***No**, I do not give permission to be contacted regarding future research participation* _____ ***Initials***