UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

University of Florida
Health Center
Institutional Review Board
APPROVED FOR USE
From 5/15/2012 Through 5/1/2013

If you are a parent, as you read the information in this Consent Form, you should put yourself in your child's place to decide whether or not to allow your child to take part in this study. Therefore, for the rest of the form, the word "you" refers to your child.

If you are an adult, child, or adolescent reading this form, the word "you" refers to you.

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

Please read this form which describes the study in some detail. A member of the research team will describe this study to you and answer all of your questions. Your participation is entirely voluntary. If you choose to participate you can change your mind at any time and withdraw from the study. You will not be penalized in any way or lose any benefits to which you would otherwise be entitled if you choose not to participate in this study or to withdraw. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study?

Long Standing Type 1 Diabetes with Residual C-peptide – A Pilot Study

3. Who do you call if you have questions about this research study?

Principal Investigator: Desmond Schatz, MD 352-273-9270

Co-Principal Investigator: Michael Haller, MD 352-273-9264

Study Coordinator: Miriam Cintron 352-273-5580

For emergencies or after hours call 352-265-0111 and ask the operator to page

Dr. Schatz or Dr. Haller.

4. Who is paying for this research study?

The sponsor of this study is The University of Michigan through an NIH (National Institute of Health) Clinical and Translational Science Award (CTSA).

5. Why is this research study being done?

The purpose of this research study is to learn more about how long people with type 1 diabetes continue to produce insulin even after having type 1 diabetes for many years. We also hope to learn more about why some people with type 1 diabetes continue to make insulin for longer periods of time than others with type 1 diabetes.

You are being asked to be in this research study because you were told by a doctor that you have type 1 diabetes (T1D) and you have had this disease for at least 5 years, but not more than 20 years. You are also between 15 and 45 years of age and no history of ketoacidosis in the past 5 years. Ketoacidosis is a combination of acid and ketones in the blood caused by lack of insulin. You must also have an A1c level under 7.5% and must take less than 0.75 units of insulin per kilogram of body weight per day. We will calculate this for you based on your recent insulin use.Your C-peptide level must be at least 0.2 nmol/L. C-peptide is a measure of the insulin being made by the cells in your pancreas.

You cannot be in this study if you are allergic to Boost, if you are taking immunosupressing mediciations (e.g., cyclosporine, imuran, or long-term systemic steroids like prednisone), if you are pregnant or breast feeding, if you have severe anemia, if you have a severe, life-threatening illness, if you are known to have HIV or liver disease , if you have a history of severe drug or alcohol abuse, or if you are treating your type 1 diabetes with glucose lowering medications other than insulin.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this research study)?

You will receive intensive insulin therapy which is considered standard of care for managing type 1 diabetes. Intensive insulin therapy means you will work closely with your diabetes treatment team to meet these goals:

- Blood sugar level before meals: 90 to 130 milligrams per deciliter (mg/dL).
- Blood sugar level two hours after meals: Less than 180 mg/dL
- Hemoglobin A1C: Less than 7 percent

To achieve these goals you will be expected to stay in good blood glucose control between each visit. You will need to take multiple daily insulin injections or use an insulin pump. You will also be expected to test your blood sugar at least 3-4 times per day. At the follow-up visit we will ask you for a record of blood glucose numbers and insulin doses before the visit.

7. What will be done only because you are in this research study?

You are being asked to take part in this CTSA multicenter study because you have been diagnosed with T1D and meet the specific study conditions.

First Visit (Screening)

This visit may take place in the Clinical Research Center (CRC) or at a clinic visit when you are scheduled to have blood drawn for routine clinical tests. At this visit, blood will need to be drawn within 4 hours after you have eaten. The blood (1 teaspoon) will be sent to a lab to measure the C-peptide and glucose (blood sugar) level. C-peptide is used to measure the insulin being made by the cells of the pancreas.

The blood (1/4 teaspoon) also will be used to measure a Hemoglobin A1c level. This is a measure of blood sugar control over the last 2 to 3 months.

We will also ask you some questions about what you do to take care of your diabetes (types of insulin you take, how often and how much), your medical history, and when you learned you had diabetes.

Second Visit (Mixed Meal Tolerance Test)

Depending on the results of your screening visit, you may be asked to return approximately 3 weeks later for a test called a 2-hour Mixed Meal Tolerance Test (MMTT). This test will only be done at the UF CRC. We will use this test to get a more exact measurement of C-peptide levels. The blood from this test will be used to measure your blood sugar levels and also for the following:

- HLA - human leukocyte antigen is an area on your chromosomes (part of your DNA) that contains a group of genes. Certain types of HLA genes are more likely to be seen in people with diabetes. The HLA type is being measured in this study to help us understand how HLA type may relate to insulin production. The amount of blood drawn is about 1/2 teaspoon.
- Diabetes-related autoantibodies - these are proteins that are made by the body's immune system. They are a sign that the cells that produce insulin could be damaged. The amount of blood drawn is less than 1 teaspoon.

In this test you will be asked to take a drink called Boost. The Boost drink is a "mixed meal" made of fats, proteins, and carbohydrates that looks like a milkshake. For three days before the MMTT, you will be asked to eat at least 150 grams of carbohydrate per day. You will get special instructions about insulin dosing the night before the test. You cannot eat or drink for about 10 hours before the test (water is allowed).

To make it easier to get the blood sample for the test, a needle and/or plastic tube (IV) will be placed in a vein in your arm. This IV will be left in place for the duration of the visit. Two blood samples taken 10 minutes apart (1 teaspoon of blood for each sample) will be drawn through the IV. You will then be given the Boost to drink.

The amount of Boost you will drink will depend on your weight (about ½ teaspoon per pound). You will be expected to drink the Boost in about 5 minutes. This drink will raise your blood sugar and cause your body to try to produce insulin. After drinking Boost, about 1 teaspoon of blood will be drawn through the IV at 15, 30, 60, 90, and 120 minutes. The total amount of blood drawn for the MMTT is 7 teaspoons.

During your visit for the MMTT, you will also be asked some questions about your diabetes and your medical history.

Blood Sample for Storage

Along with the tests described above and with your permission, we will store a sample of your blood indefinitely. This sample will be used to learn more about how the immune system might cause diabetes. We might also learn about new ways of finding out if people are at risk of T1D. We will get the blood for this test through the IV that is already in place for the MMTT. The total amount of blood we will need for storage will not be more than 6 teaspoons and the amount we take will be based on your weight.

If you have any questions now or at any time during the study, please contact one of the research team members listed in question 3 of this form.

Amount of Blood to Be Drawn

All together, we will never take more blood than is safe for your age and weight. The exact amount we take will depend on your age, weight, and whether an MMTT test is done. For adults, the maximum amount of blood taken in a 1 month period will be about 16 teaspoons. For children under age 18, the maximum amount taken in a 1 month period will not be more than about 1/2 teaspoon for each pound of body weight. For example, the maximum amount taken in a 1 month period for a child weighing 55 lbs will be a little more than 8 teaspoons.

8. How long will you be in this research study?

You will be in the study for less than 4 months. The screening visit should not take more than 1 hour. The MMTT visit will be about 4 hours long. See below for your visit schedule

Procedure	Baseline	MMTT
Informed Consent	X	
Clinical Information	X	
Non-fasting C-peptide and Glucose	X	
Autoantibodies		X
HLA typing		X
HbA1c	X	
Mechanistic samples		X

9. How many people are expected to take part in this research study?

We expect to enroll approximately 200 subjects from 7 CTSA centers in the United States. At the University of Florida we may need to screen up to 100 subjects to get to the 10 subjects needed for study completion.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

10. What are the possible discomforts and risks from taking part in this research study?

The risks of drawing blood from a vein include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection; and, uncommonly, faintness from the procedure. If necessary a numbing ointment can be applied to the place the needle goes in to minimize discomfort.

There are no known risks to the MMTT, but you may not like the taste of the Boost drink. Some people who drink Boost may experience minor symptoms during the MMTT test such as feeling nauseated. To avoid a low blood sugar, do not participate in any physical activity before the MMTT. Occasionally someone may have low blood sugar or high blood sugar after the test, if insulin has been adjusted before or after the test. Blood glucose will be monitored before and during testing. The glucose value after the test will be checked and appropriate insulin dosage adjustments will be made. Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 17-21 in this form discuss what information about you will be collected, used, protected, and shared.

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

Participation in more than one research study or project may further increase the risks to you. If you are already enrolled in another research study, please inform one of the research team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Additional information can be obtained at: http://irb.ufl.edu/gina.html or call 1-800-669-3362. If you think this law has been violated, it will be up to you to pursue any compensation from the offending insurance company and/or employer.

Throughout the study, the researchers will notify you of new information that may become available and might affect your decision to remain in the study.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the research team members listed in question 3 in this form.

11a. What are the potential benefits to you for taking part in this research study?

There is no direct benefit to you for participating in this research study. We will provide you and your study doctor with your C-peptide, autoantibody, and MMTT test results. These test results may or may not be useful to your physician in caring for you. You and your study doctor will not be given any other test results.

11b. How could others possibly benefit from this study?

Information gained from this research study may increase knowledge about the treatment and prevention of T1D in the future.

11c. How could the researchers benefit from this study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator listed in question 3 of this form may benefit if the results of this study are presented at scientific meetings or in scientific journals.

12. What other choices do you have if you do not want to be in this study?

You are not required to take part in this study. You can choose not to participate, and you can continue your routine diabetes care whether or not you participate. There may be other trials for people with T1D being done elsewhere.

13a. Can you withdraw from this study?

You are free to withdraw your consent and to stop participating in this study at any time. If you do withdraw your consent, you will not be penalized in any way and you will not lose any benefits to which you are entitled.

If you decide to withdraw your consent to participate in this study for any reason, please contact one of the research team members listed in question 3 of this form. They will tell you how to stop your participation safely.

If you have any questions regarding your rights as a research subject, please call the Institutional Review Board (IRB) office at (352) 273-9600.

13b. If you withdraw, can information about you still be used and/or collected?

If you leave the study early for any reason, the information that has already been collected will remain in the study database, but no further information will be collected for the study.

13c. Can the Principal Investigator withdraw you from this study?

You may be withdrawn from the study without your consent for the following reasons:

- It is determined that you are not eligible for the study.
- The study is stopped.
- There are unanticipated circumstances.
- The Principal Investigator feels that you have not followed instructions given to you.
- You become pregnant.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

14. If you choose to take part in this research study, will it cost you anything?

Boost® will be provided at no cost to you while you are participating in this study.

The Sponsor will pay for all medical services or activities required as part of your participation in this study as described above in the question "What Will Be Done Only Because You Are In This Research Study".

If you receive a bill for these services, please contact Desmond Schatz, MD 352-273- 9270 or Miriam Cintron 352-273-5580.

All other medical services you receive would have been provided to you even if you were not in the study. These services will be billed to you or your insurance company. You will be responsible for paying any deductible, co-insurance, and/or co-payments for these services, and any non-covered or out-of-network services.

Some insurance companies may not cover costs associated with studies. Please contact your insurance company for additional information.

15. Will you be paid for taking part in this study?

As compensation for travel and other expenses, you will receive $25 for having the one-time blood draw and providing information on your diabetes and health at the first study visit. If you have a MMTT as a part of this study, you will be paid $50 for completed MMTT visit. You will be given a parking voucher to cover your parking costs for all visits.

In order to process your payment, you will need to give us your name, address and social security number. This information will be sent to the appropriate University employees for the purpose of making and recording the payment. Your check will be sent to you by the University of Florida. You do have the option of declining payment.

16. What if you are injured because of the study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

No additional compensation is offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact 352-265-0111 and ask the operator to page Dr. Schatz or Dr. Haller if you experience an injury or have questions about any discomforts that you experience while participating in this study.

17. How will your health information be collected, used and shared?

If you agree to participate in this study, the Principal Investigator will create, collect, and use private information about you and your health. This information is called protected health information or PHI. In order to do this, the Principal Investigator needs your authorization The following section describes what PHI will be collected, used and shared, how it will be collected, used, and shared, who will collect, use or share it, who will have access to it, how it will be secured, and what your rights are to revoke this authorization.

Your protected health information may be collected, used, and shared with others to determine if you can participate in the study, and then as part of your participation in the study. This information can be gathered from you or your past, current or future health records, from procedures such as physical examinations, x-rays, blood or urine tests or from other procedures or tests. This information will be created by receiving study treatments or participating in study procedures, or from your study visits and telephone calls. More specifically, the following information may be collected, used, and shared with others:

- Demographic information

- Complete past and present medical history
- Family medical history related to autoimmune disease
- Related laboratory results
- Records of physical exams
- Treatment/management of T1D
- Use of devices (e.g., insulin pump, continuous glucose monitor, glucose meter)
- Acute complications such as severe hypoglycemia and diabetic ketoacidosis
- Testing results of this study

This information will be stored in locked filing cabinets at the University of Florida and on computer servers with secure passwords, or encrypted electronic storage devices.

Some of the information collected could be included in a "limited data set" to be used for other research purposes. If so, the limited data set will only include information that does not directly identify you. For example, the limited data set cannot include your name, address, telephone number, social security number, photographs, or other codes that link you to the information in the limited data set. If limited data sets are created and used, agreements between the parties creating and receiving the limited data set are required in order to protect your identity and confidentiality and privacy.

18. For what study-related purposes will your protected health information be collected, used, and shared with others?

Your PHI may be collected, used, and shared with others to make sure you can participate in the research, through your participation in the research, and to evaluate the results of the research study. More specifically, your PHI may be collected, used, and shared with others for the following study-related purpose(s):

- To learn if you are still producing your own insulin
- To learn how C-peptide levels in the blood are related to how long you have had T1D
- To learn how C-peptide levels in the blood are related to characteristics such as glycemic control, HLA type, and autoantibody status
- To collect specimen samples to further understanding of T1D and its complications

Once this information is collected, it becomes part of the research record for this study.

19. Who will be allowed to collect, use, and share your protected health information?

Only certain people have the legal right to collect, use and share your research records, and they will protect the privacy and security of these records to the extent the law allows. These people include:

- the study Principal Investigator (listed in question 3 of this form) and research staff associated with this project.
- other professionals at the University of Florida or Shands Hospital that provide study-related treatment or procedures.
- the University of Florida Institutional Review Board (IRB; an IRB is a group of people who are responsible for looking after the rights and welfare of people taking part in research).

20. Once collected or used, who may your protected health information be shared with?

Your PHI may be shared with:

- the study sponsor (listed in Question 4 of this form).
- the centers associated with this Clinical and Translational Science Award (CTSA) will have access to your C-peptide data. This information will be used to document the presence or absence of C-peptide in other patients with T1D.
- United States and foreign governmental agencies who are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections .
- Government agencies who are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.

Otherwise, your research records will not be released without your permission unless required by law or a court order. It is possible that once this information is shared with authorized persons, it could be shared by the persons or agencies who receive it and it would no longer be protected by the federal medical privacy law.

21. If you agree to take part in this research study, how long will your protected health information be used and shared with others?

Your PHI will be used and shared with others until the end of the study.

You are not required to sign this consent and authorization or allow researchers to collect, use and share your PHI. Your refusal to sign will not affect your treatment, payment, enrollment, or eligibility for any benefits outside this research study. However, you cannot participate in this research unless you allow the collection, use and sharing of your protected health information by signing this consent and authorization.

You have the right to review and copy your protected health information. However, we can make this available only after the study is finished.

You can revoke your authorization at any time before, during, or after your participation in this study. If you revoke it, no new information will be collected about

you. However, information that was already collected may still be used and shared with others if the researchers have relied on it to complete the research. You can revoke your authorization by giving a written request with your signature on it to the Principal Investigator.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent & Authorization Date

Consenting Adults. You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask other questions at any time.

Adult Consenting for Self. By signing this form, you voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described in sections 17-21 above. By signing this form, you are not waiving any of your legal rights.

Signature of Adult Consenting & Authorizing for Self Date

Parent/Adult Legally Representing the Subject. By signing this form, you voluntarily give your permission for the person named below to participate in this study. You hereby authorize the collection, use and sharing of protected health information for the person named below as described in sections 17-21 above. You are not waiving any legal rights for yourself or the person you are legally representing. After your signature, please print your name and your relationship to the subject.

Consent & Authorization Signature of Parent/Legal Representative Date

Print: Name of Legal Representative

Print: Relationship to Participant:

Print: Name of Subject:

Participants Who Cannot Consent But Can Read and/or Understand about the Study. Although legally you cannot "consent" to be in this study, we need to know if you want to take part. If you decide to take part in this study, and your parent or the person legally responsible for you gives permission, you both need to sign. Your signing below means that you agree to take part (assent). The signature of your parent/legal representative above means he or she gives permission (consent) for you to take part.

Assent Signature of Participant	Date

CONSENT TO COLLECT AND STORE TISSUE FOR FUTURE RESEARCH WHEN IDENTITY OF SUBJECT IS CODED AND THE CODES ARE KEPT IN LOCKED FILES BY THE PERSON CONDUCTING THE RESEARCH

As part of the research project "Long Standing Type 1 Diabetes with Residual C-peptide – A Pilot Study"– Dr. Schatz and Dr. Haller would like to store some of your blood tissue that is not needed for your medical treatment and that would otherwise be thrown away. If you agree, Dr. Schatz and Dr. Haller will keep the samples in a specimen bank so that they may be used in future research to learn more about diabetes and other medical problems. Researchers are trying to learn more about diabetes, such as what causes diabetes, how to prevent it, how to treat it better, and how, hopefully, to cure it. Even if the research that is done on your tissue cannot be used to help you, it might help other people who have diabetes or other medical problems.

Many medical problems may arise due to the environment or from genetic factors. Your diabetes may come from one or both of these causes. Genetic factors are those that people are born with and that can affect other family members. There may be genetic testing done in the future that would provide information about traits that were passed on to you from your parents or from you to your children.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Additional information can be obtained at: http://irb.ufl.edu/gina.html or call 1-800-669-3362. If you think this law has been violated, it will be up to you to pursue any compensation from the offending insurance company and/or employer.

Dr. Schatz, or his/her successor, will be responsible for making sure that your samples are protected in the specimen bank and that your medical information is kept confidential. Your samples will not be stored with your name or other identifying information but instead will be given a code number to protect your identity. The samples and this code number will only be given to researchers whose research is approved by the Institutional Review Board (IRB). (An IRB is a group of people who are responsible for looking after the rights and welfare of people taking part in research). The researchers will not be told who you are. Because the nature and value of any future research cannot be known at this time, any results obtained from using your tissue will not be given to you or your doctor.

The people who use your samples to do research may need to know more about your health. If researchers ask for reports about your health (information from your medical records), Dr. Schatz and Dr. Haller will not give them or anyone else your name, address, or phone number (unless you are willing to be contacted in the future to take part in more research). Although every effort will be made to keep your information confidential, there is a small risk that an unauthorized person may review your information. Therefore, there is a very slight risk that a test result could be linked to your identity and inadvertently disclosed to you or to a third party. If you were to receive the

result of a genetic test that indicated a problem, it could cause anxiety or other psychological distress. In addition, you might have to decide whether or not to discuss the findings with members of your family. If a third party (like your employer or insurer) learned the results, there is a risk of discrimination that could affect your employability or insurability, of stigma, and of the unpredicted disclosure of this information to others. You can discuss these issues further with your doctor or nurse and you can request a consultation with a genetic counselor if you wish to discuss these possible risks. In addition, there are laws that require that research records that have your name on them may be shown to people who make sure that the research is being done correctly. As mentioned in the accompanying consent form, the NIH, FDA, and the Institutional Review Board have the legal right to review and copy your medical records related to this research.

There will be no cost to you for any specimens collected and stored in the specimen storage bank. Your tissue will be used only for research and will not be sold. Some new products might be made because of the results of the research that uses your samples. These products might be sold sometime in the future, but, should this occur, you will not get paid.

The choice to let Dr. Schatz and Dr. Haller keep your tissue for doing research is entirely up to you. No matter what you decide to do, it will not affect your care. If you decide that your tissue can be kept for research but you later change your mind, tell Dr. Dr. Schatz and Dr. Haller who will remove and destroy any of your tissue that he/she still has. Otherwise, the samples may be kept until they are used up, or until Dr. Schatz and Dr. Haller decides to destroy them.

Please review statements 1, 2, 3, and 4 and then circle the answer that is right for you. If you have questions, please talk to your doctor or nurse.

1. I agree that my samples may be stored, coded to protect my identity, and that my identity will not be disclosed to anyone without my permission, except when required by law.
   YES NO Initials_____

2. I agree that some excess blood tissue may be kept by Dr. Schatz and Dr. Haller for use in future research to learn about, prevent, treat, or cure diabetes
   YES NO Initials_____

3. I agree that my blood tissue may be used for research to answer other medical questions that are not necessarily related to diabetes
   YES NO Initials_____

4. I agree that my doctor (or someone he/she chooses) can contact me in the future to ask me to take part in more research.
   YES NO Initials_____