IRB USE ONLY
Approval Date: August 6, 2013
Expiration Date: August 6, 2014

Please check one of the following:

_____ You are an adult participant in this study.

_____ You are the parent or guardian granting permission for a child in this study.

Print child's name here:

_____

The following information applies to the adult participant or to the child or ward. If the participant is a child or ward, the use of "you" refers to "your child" or "your ward."

****

Are you participating in any other research studies? _____ Yes _____No

PURPOSE OF RESEARCH

You recently participated in a TrialNet study. As you know, TrialNet is an international research group dedicated to the study, prevention, and early treatment of type 1 diabetes.

You were selected as a possible participant in this study because you were either in a TrialNet study before you were diagnosed with type 1 diabetes, or you were in a TrialNet study that started soon after you developed diabetes. These studies have provided important information about how diabetes develops and the effects of different therapies.

You are now being invited to participate in a follow-up study so that we can continue to learn from you. We hope to learn whether there are long-term effects of any experimental treatment you may have received. We also hope to learn whether participating in a TrialNet study has affected what happens to your diabetes over time whether or not you received experimental therapy.

We are particularly interested in finding out about your general health, your diabetes, and how much insulin you make over time.

IRB USE ONLY
Approval Date: August 6, 2013
Expiration Date: August 6, 2014

This research study is looking for people who have type 1 diabetes and previously participated in another TrialNet study. TrialNet is looking for approximately 1800 people nationwide. Stanford University expects to enroll approximately 100 research study participants.

VOLUNTARY PARTICIPATION

Your participation in this study is entirely voluntary. Your decision not to participate will not have any negative effect on you or your medical care. You can decide to participate now, but withdraw your consent later and stop being in the study without any loss of benefits or medical care to which you are entitled.

DURATION OF STUDY INVOLVEMENT

This research study is expected to last for several years. It is your choice to be in the study, and you can stop participating at any time.

PROCEDURES

If your previous TrialNet study results show that you are still making insulin you will be asked to come in every six months to measure your insulin secretion. Insulin secretion is measured by an Oral Glucose Tolerance Test (OGTT) or a Mixed Meal Tolerance Test (MMTT).

- For those in TrialNet studies **before** their diagnosis of diabetes, you will be asked to do either an OGTT *or* an MMTT at study visits. At the visit one year after your diagnosis, you will be asked to do both tests. These will be done on two separate days.
- For those who started in a TrialNet study **after** diagnosis, you will be asked to do a MMTT at each study visit.

At any time we find that you no longer make insulin, you will not be asked to do any further OGTT or MMTT testing. You will then just be contacted annually. We may be able to arrange for you to have a blood sample taken at a location convenient to you.

For all participants, the blood samples will be used to measure HbA1c and do other studies to learn about your general health and immune system. We will also ask you questions about your diabetes management and general health.

All together, the studies will require about 2 tablespoons of blood in adults at each visit. Less blood may be taken from children depending upon their age and weight. The total amount of blood drawn for tests at each visit will not exceed limits that are safe for your age and weight. Each visit will take about 3 hours.

The tests are described here:

- **MMTT and OGTT**

You will need to be fasting on the day of your test. Before each MMTT or OGTT, you will get special instructions about diet and insulin dosing. To make the blood sampling easier for the test, an intravenous needle and plastic tube (IV) will be placed in your vein. The IV will be kept in place during the test. Two blood samples taken ten minutes apart (one teaspoon of blood for each sample) will be taken through the IV. You will then drink either a sweet liquid that contains glucose for the OGTT, or a drink called Boost which has glucose as well as fats and proteins for the MMTT. Blood samples will be drawn through the IV at regular intervals for 2 hours.

If you are asked to do both an MMTT and OGTT, they will need to be performed on separate days.

- **HbA1c Test**

This blood test measures a person's average blood glucose level for last 2-3 months before the test.

- **Blood Samples for Understanding Type 1 Diabetes**

Blood samples may be obtained to better understand how type 1 diabetes progresses and to get ideas about new treatments in the future. While TrialNet is ongoing, these samples will be used only by TrialNet approved researchers. As such, we may be collecting blood samples including genetic samples for these studies at most of your visits. You will not routinely be provided with test results from these studies. We will discuss with you the type of tests to be done.

Most of the time the study will require about 1- 2 tablespoons of blood in adults. We will let you know about how much blood we need to take. We will not take more than is safe. For those under age 18, we will not take more than is safe for your age and weight.

- **Additional Information**

You will be offered the results of your OGTT, MMTT and HbA1C testing soon after each visit. You may have the option of going to another study site for follow-up if it is more convenient for you. If so, your contact information will be shared with other TrialNet investigators to make arrangements for you to be followed at another study site.

Your samples will be sent outside of Stanford for analysis to TrialNet-approved labs.

Any of your samples which are used in research may result in new products, tests or discoveries. In some instances, these may have potential commercial value and may be developed and owned

by the Investigators, Stanford University and/or others. However, donors of samples do not retain any property rights to the materials. Therefore, you would not share in any financial benefits from these products, tests or discoveries.

Tissue Sampling for Research

Research using tissues is an important way to try to understand human disease. You have been given this information because the investigators want to include your tissues in a research project and because they want to save the samples for future research. There are several things you should know before allowing your tissues to be studied.

Storage of Samples in NIDDK Repository

When TrialNet is over, we intend to put any remaining samples, including genetic samples, into the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) repository for future studies related to type 1 diabetes and its complications. They will be stored there indefinitely without your name or any other identifying information on them, and, as such, once in the repository you will not be able to have them removed. Researchers must first get permission from the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) to use samples from the repository.

You have the right to refuse to allow your tissues to be studied now or saved for future study. You may withdraw from this study at any time. The investigators might retain the identified samples, e.g., as part of your routine clinical care, but not for additional research.

The following checkbox gives you the choice of allowing us to put any remaining blood samples in the NIDDK repository. Even if you decide not to have your remaining blood samples stored, you can still participate in this study.

Are you willing to allow us to put any remaining blood samples in the NIDDK repository (please initial yes or no)?

_____YES _____NO

Tissue Sampling for Genetic Testing

As part of the analysis on your samples, the investigators may do genetic testing. Genetic research is research that studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications and responses to treatment. Genetic research raises

certain questions about informing you of any results. Possible risks of knowing results include: anxiety; other psychological distress; and the possibility of insurance and job discrimination. A possible risk of not knowing includes being unaware of the need for treatment. These risks can change depending on the results of the research and whether there is a treatment or cure for a particular disease.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against you based on your genetic information.

The results of the study of your samples from this project will be used for research purposes only, and you will not be told the results of the tests.

PARTICIPANT RESPONSIBILITIES

As a participant, your responsibilities include:

- Follow the instructions of the Protocol Director and study staff.
- Keep your study appointments. If it is necessary to miss an appointment, please contact the Protocol Director or research study staff to reschedule as soon as you know you will miss the appointment.
- Tell the Protocol Director or research study staff about any side effects, doctor visits, or hospitalizations that you may have.
- Tell the Protocol Director or research staff if you believe you might be pregnant.
- Ask questions as you think of them.
- Tell the Protocol Director or research staff if you change your mind about staying in the study.

WITHDRAWAL FROM STUDY

If you first agree to participate and then you change your mind, you are free to withdraw your consent and discontinue your participation at any time. Your decision will not affect your ability to receive medical care for your disease and you will not lose any benefits to which you would otherwise be entitled.
If you decide to withdraw your consent to participate in this study, you should notify Dr. Darrell Wilson at (650)723-5791.

The Protocol Director may also withdraw you from the study without your consent for one or more of the following reasons

- Failure to follow the instructions of the Protocol Director and study staff.
- The Protocol Director decides that continuing your participation could be harmful to you.
- Pregnancy
- You need treatment not allowed in the study.
- The study is cancelled.
- Other administrative reasons.
- Unanticipated circumstances.

POSSIBLE RISKS, DISCOMFORTS, AND INCONVENIENCES

There are risks, discomforts, and inconveniences associated with any research study. These deserve careful thought. You should talk with the Protocol Director if you have any questions.

You could have discomfort and/or a bruise when you get your blood drawn. Once in a while, some people may faint. It is rare, but some people may get an infection, a small blood clot, swelling of the vein and surrounding tissue or bleeding where the needle enters the skin. Some people may feel nauseous when they have the OGTT. The use of Boost during the MMTT has no known side effects, but you may not like the taste. There may be risks to you which are currently unforeseeable.

If you must travel a distance to get to your study visits, you may feel inconvenienced.

POTENTIAL BENEFITS

During the study we will share with you information about your health and diabetes. We cannot and do not guarantee or promise that you will receive any benefits from this study.

ALTERNATIVES

You can choose not to participate in this study.

PARTICIPANT'S RIGHTS

You should not feel obligated to agree to participate. Your questions should be answered clearly and to your satisfaction. If you decide not to participate, tell the Protocol Director.

You will be told of any important new information that is learned during the course of this research study, which might affect your condition or your willingness to continue participation in this study.

CONFIDENTIALITY

Your identity will be kept as confidential as possible as required by law. Your personal health information related to this study may be disclosed as authorized by you. Your research records may be disclosed outside of Stanford, but in this case, you will be identified only by a unique code number. It will identify the information and samples collected from you from study examinations and procedures. It will be sent to the central TrialNet Coordinating Center at the University of South Florida.
Information about the code will be kept in a secure location and access limited to research study personnel.

Patient information may be provided to Federal and other regulatory agencies as required. The Food and Drug Administration (FDA), for example, may inspect research records and learn your identity if this study falls within its jurisdiction.

Personal information is information such as your name that directly identifies you. This personal information will be kept in a database at the central TrialNet Coordinating Center as sanctioned by the NIDDK. We may share your personal information with other TrialNet study investigators to help you participate.

When TrialNet is completed, your data (but not your personal identifying information) will be moved to another location that will be under the supervision of the NIDDK. Once this happens, it will no longer be possible to link your code to your name or other personal identifying information.

A Certificate of Confidentiality has been obtained from the National Institutes of Health (NIH). This is intended to further protect the confidentiality of information that we obtain about you. By having a Certificate of Confidentiality, TrialNet researchers are not required to give information that can be used to identify you. For example, we cannot be forced to give information about you to insurance companies. Also, we cannot be forced to give information about you for any civil, criminal, administrative, or legislative proceedings whether at the federal, state or local level. However, the Certificate of Confidentiality does not prevent you from giving this information to others. Please understand that we will maintain the confidentiality of your research record. We cannot guarantee the confidentiality of test results provided to you if you wish to share them.

There are some rare exceptions to the protection offered by the Certificate of Confidentiality. TrialNet researchers are not prevented from telling about matters such as child abuse, certain infectious diseases, or threatened violence to yourself or others.

TrialNet researchers will consider your records private. Rarely, representatives of the United States Department of Health and Human Services (DHHS) or TrialNet may review or ask for a copy of your study records. If this happens, we will provide your records. Also, for auditing purposes, employees of Stanford University or its agents could be allowed to see your study records to make sure that the study is being done properly.

The results of this study may be published for scientific purposes. By signing this form, you are agreeing to this. Your records and results will not be identified as belonging to you in any publication

IRB USE ONLY
Approval Date: August 6, 2013
Expiration Date: August 6, 2014

Authorization To Use Your Health Information For Research Purposes

Because information about you and your health is personal and private, it generally cannot be used in this research study without your written authorization. If you sign this form, it will provide that authorization. The form is intended to inform you about how your health information will be used or disclosed in the study. Your information will only be used in accordance with this authorization form and the informed consent form and as required or allowed by law. Please read it carefully before signing it.

What is the purpose of this research study and how will my health information be utilized in the study?

You were either in a TrialNet study before you were diagnosed with type 1 diabetes, or you were in a TrialNet study that started soon after you developed diabetes. These studies have provided important information about how diabetes develops and the effects of different therapies.

You are now being asked to participate in a follow-up study so that we can continue to learn from you. We hope to learn whether there are long-term effects of any experimental treatment you may have received. We also hope to learn whether participating in a TrialNet study has affected what happens to your diabetes over time whether or not you received experimental therapy.

We are particularly interested in finding out about your general health, your diabetes, and how much insulin you make over time.

Do I have to sign this authorization form?

You do not have to sign this authorization form. But if you do not, you will not be able to participate in this research study.
Signing the form is not a condition for receiving any medical care outside the study.

If I sign, can I revoke it or withdraw from the research later?

If you decide to participate, you are free to withdraw your authorization regarding the use and disclosure of your health information (and to discontinue any other participation in the study) at any time. After any revocation, your health information will no longer be used or disclosed in the study, except to the extent that the law allows us to continue using your information (e.g., necessary to maintain integrity of research). If you wish to revoke your authorization for the research use or disclosure of your health information in this study, you must write to: Darrell Wilson, MD, 300 Pasteur Drive, G313, Stanford, CA 94305.

What Personal Information Will Be Obtained, Used or Disclosed?

Your health information related to this study may be used or disclosed in connection with this research study, including, but not limited to your diabetes status, HbA1C, results of glucose tolerance testing, and blood testing to better understand how type 1 diabetes progressed.

Who May Use or Disclose the Information?

The following parties are authorized to use and/or disclose your health information in connection with this research study:

- The Protocol Director, Darrell Wilson, MD
- The Stanford University Administrative Panel on Human Subjects in Medical Research and any other unit of Stanford University as necessary
- Research Staff
- Other members of the TrialNet study team at Stanford University

Who May Receive or Use the Information?

The parties listed in the preceding paragraph may disclose your health information to the following persons and organizations for their use in connection with this research study:

- The Office for Human Research Protections in the U.S. Department of Health and Human Services
- The National Institutes of Health, and other federal and state agencies as required by law
- TrialNet Data Safety Monitoring Board

- Other members of the TrialNet team at the other study sites and the data collection centers

Your information may be re-disclosed by the recipients described above, if they are not required by law to protect the privacy of the information.

When will my authorization expire?
Your authorization for the use and/or disclosure of your health information will end on July 31, 2112 or when the research project ends, whichever is earlier.

_____ _____
Signature of Participant Date

-OR-

_____ _____
Signature of Legally Authorized Representative Date

_____
Description of Representative's Authority to Act for Subject

FINANCIAL CONSIDERATIONS

Payment

You will be paid $50 per visit that includes an OGTT or MMTT, or $25 per visit that does not include an OGTT or MMTT. We will also pay a small amount for travel and parking costs.

Payments may only be made to U.S. citizens, legal resident aliens, and those who have a work eligible visa. You may need to provide your social security number to receive payment.

Costs

There is no cost to you for participating in this study.

Sponsor

This study is sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), with additional sponsorship by the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Child Health and Human Development (NICHD), and the National Center for Research Resources (NCRR). Other support is from the Juvenile Diabetes Research Foundation and the American Diabetes Association.

The National Institutes of Health are providing some financial support for the facility and staff where part or all of the study is taking place.

COMPENSATION for Research-Related Injury

All forms of medical diagnosis and treatment – whether routine or experimental– involve some risk of injury. In spite of all precautions, you might develop medical complications from participating in this study. If such complications arise, the Protocol Director and the research study staff will assist you in obtaining appropriate medical treatment. In the event that you have an injury or illness that is directly caused by your participation in this study, reimbursement for all related costs of care first will be sought from your insurer, managed care plan, or other benefits program. **You will be responsible for any associated co-payments or deductibles as required by your insurance.**

If costs of care related to such an injury are not covered by your insurer, managed care plan or other benefits program, you may be responsible for these costs. If you are unable to pay for such costs, the Protocol Director will assist you in applying for supplemental benefits and explain how to apply for patient financial assistance from the hospital.

You do not waive any liability rights for personal injury by signing this form.

CONTACT INFORMATION

Questions, Concerns, or Complaints: If you have any questions, concerns or complaints about this research study, its procedures, risks and benefits, or alternative courses of treatment, you should ask the Protocol Director, Darrell Wilson, MD. You may contact him now or later at (650) 723-5791. You should also contact him at any time if you feel you have been hurt by being a part of this study.

Independent Contact: If you are not satisfied with how this study is being conducted, or if you have any concerns, complaints, or general questions about the research or your rights as a participant, please contact the Stanford Institutional Review Board (IRB) to speak to someone independent of the research team at (650)-723-5244 or toll free at 1-866-680-2906. You can also write to the Stanford IRB, Stanford University, MC 5579, Palo Alto, CA 94304.

Appointment Contact: If you need to change your appointment, please contact Trudy Esrey, RD, at (650) 498-4450. You may also contact her if you cannot reach the Protocol Director.

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

As a research participant you have the following rights. These rights include but are not limited to the participant's right to:

- be informed of the nature and purpose of the experiment;
- be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized;
- be given a description of any attendant discomforts and risks reasonably to be expected;
- be given an explanation of any benefits to the subject reasonably to be expected, if applicable;
- be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;
- be informed of the avenues of medical treatment, if any available to the subject after the experiment if complications should arise;
- be given an opportunity to ask questions concerning the experiment or the procedures involved;
- be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice;
- be given a copy of the signed and dated consent form; and

- be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

May we contact you about future studies that may be of interest to you?
____ Yes ____ No

Signing your name means you agree to be in this study and that you were given a copy of this consent form.

_____ _____
Signature of Adult Participant Date

-OR-

_____ _____
Signature of LAR (Parent, Guardian or Conservator) Date

_____
Authority to act for participant

_____ _____
(If available) Signature of Other Parent or Guardian Date

_____
Authority to act for participant

The IRB determined that the permission of one parent is sufficient for research to be conducted under 45 CFR 46.404, in accordance with 45 CFR 46.408(b).

_____ _____
Signature of Person Obtaining Consent Date

IRB USE ONLY
Approval Date: August 6, 2013
Expiration Date: August 6, 2014

Participant ID:

STUDY