Date: **Valid for Use Through:**

Treatment Consent Form

Study Title: The Restoring Insulin Secretion (RISE) Study Pediatric Protocol: Treatment phase consent

Principal Investigator:
Version Date: 05/21/2013

You (you = you or your child) are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Why is this study being done?

You are being asked to take part in a research study to see if medications used for the treatment of type 2 diabetes can help the body to make insulin or slow the progression of prediabetes or early type 2 diabetes in teenagers. It is currently thought that the best time to slow or stop diabetes is at its earliest stages. This study is called the RISE Pediatric Study.

Metformin is a pill approved by the FDA for treating type 2 diabetes in children. Insulin glargine is a once a day injection approved for treating type 2 diabetes in adults, and type 1 diabetes in children. We received special approval from the Food and Drug Administration for use of glargine and metformin for this study.

You are being asked to participate in the treatment phase of the RISE Pediatric Study because you are between the ages of 10 and 19, you have prediabetes or early type 2 diabetes, and have completed the screening phase of the study.

Other people in this study

Up to 40 participants will be enrolled in this study in xx and up to 120 total at 4 pediatric sites across the US. The study is expected to last 5 years, but your will part will last for only 21 months.

What will happen during the treatment phase?

The table at the end of this form lists all the procedures that will be done during this study.

If you continue in the treatment phase of the RISE study, you will participate in three (3) long study visits, two (2) medium visits, and three (3) shorter study visits over 21 months. At the beginning of the RISE study, you will be placed in one of two treatment groups:

- Group 1 will start or continue on metformin.
- Group 2 will start insulin glargine, followed by metformin.

This study will have two different groups of research subjects like you. To decide which group you will be in, we will use a method of chance. This method is like flipping a coin or rolling dice. Each group will get slightly different care. You will not know which treatment group you are in. Neither will your study doctor. This information needs to be kept secret so that the study is based on scientific results, not on peoples' opinions.

However, we can give this information out if you have an emergency. If you are in an emergency, make sure you tell the emergency staff about this study. They can contact us, and we will give them all relevant information.

1. *Metformin:*
   If you are randomized into the metformin treatment group, and if you were on metformin before you entered RISE, the dose will gradually be increased to a maximum of 1 tablet twice daily. You will take metformin for 12 months. We will adjust the dose as tolerated.

2. *Insulin glargine followed by metformin*
   Insulin glargine is a slow release, long acting form of insulin given once a day. This type of insulin works similarly to the way your pancreas releases insulin when you are not eating. You will take the glargine by injection one time per day. You will monitor your blood sugar using a home blood glucose monitor that will be provided to you. You will be trained on when and how to check your blood sugar levels. We will start you on a small dose of glargine and over a period of 1 month, we will adjust your glargine dose to a fasting meter glucose level of 85-95 mg/dl. You will continue the glargine treatment for a total of 3 months.

   After discontinuing the glargine, you will begin to take metformin at a dose of one half tablet (500 mg) per day. The metformin dose will gradually be increased over a month to a maximum of 1000 mg twice daily (One pill, twice a day, for a total of 2 pills per day).The metformin treatment will last 9 months to bring the total duration of treatment to 12 months.

RISE Study Visits

If you choose to join the RISE Study treatment phase, you will be seen every 3 months throughout the study for a total of 8 visits. During the first 12 months of the study, you will receive treatment according to the group to which you have been assigned. The body's ability to produce insulin will be measured and diabetes tests will be run at the beginning of the study, 6 months later (Visit 3), and 12 months later (Visit 5). Three and 9 months after you stop taking the study medication, we will once again measure your body's ability to make insulin and give you diabetes tests (Visits 6 and 8).

1. Study Visit 1 -

This visit will take around one and a half days and will include an overnight stay in the research center**:**

- You will be asked not to eat or drink anything but water for at least 10 hours before the visit.
- You will be asked to come to the research center before 8 AM in the morning.
- We will measure your height and weight, as well as your waist and hip measurements using a tape measure. Blood pressure will be checked using a cuff that inflates around your arm.
- You will be asked about any changes to your health and/or medications since your last visit.
- We will do a brief physical exam, including an exam of your pubertal maturation.
- If you are female and you are old enough, you will be asked to give a urine sample for a pregnancy test. You cannot continue to be on the study if you are pregnant.
- A small plastic needle will be inserted in a vein on one of your hands or arms (we call this an IV) for drawing blood samples. This area will be kept warm with a heating pad to improve the blood circulation. If you would like, we will use numbing medicine before placing the IV.
- An oral glucose tolerance test (OGTT) will be performed. Two blood samples will be taken from your arm to test your blood sugar and other blood tests related to diabetes and heart disease. You will then be asked to drink a glassful of flavored sugar water over 5 minutes. Blood samples will be taken from your hand IV every 10 to 30 minutes for a total of 8 times. The test will last 3 hours. The total amount of blood drawn for this test will be about 8 tablespoons.
- At the end of the test you will be given lunch.
- You will spend the rest of the day in the research center eating meals provided by the study.

- You will be asked to fill out questionnaires related to sleep.
- You will be asked not to eat or drink anything but water for at least 10 hours before the visit.
- The next morning, a second IV will be placed on your opposite arm for a test called a hyperglycemic or glucose clamp which measures how well your pancreas produces insulin while you receive IV glucose. If the first IV is no longer working, there is a chance it will have to be replaced. At approximately 8:00 AM, the glucose clamp test will begin and last until approximately 12:00 PM. More information about this test is given later in this consent form. After the clamp test, you will be given lunch and the IV's removed once your blood sugar is stable.
- You will be provided with a 3 month supply of study medications and a logbook.
- Your blood sugars will be reviewed and any questions answered
- You will go home after you have eaten lunch and your blood sugar is stable.
- The study staff will be in contact with you to review blood sugars and answer any questions you may have after the visit.

2. Study Visit 2 - 3 months after Visit 1

This visit will last around 1 hour.

- You will be asked to bring your meter, logbook, study medication bottles and cartridges. This applies to all participants in the study.
- You will have a physical exam including height, weight and blood pressure.
- You will be asked about changes in your health since your last visit.
- You will have about 1 tablespoon of blood drawn to check your blood sugar level and a test called HbA1C which measures glucose control over the last 3 months.
- Your blood sugars will be reviewed and your questions answered.
- You will receive refills of your study medication.
- If you are female and you are old enough, a urine pregnancy test will be done.

3. Study Visit 3 - 6 months after Visit 1

This visit will take around 4 hours.

- You will be asked not to eat or drink anything but water for at least 10 hours before we see you.
- You will be asked to bring your meter, logbook, study medication bottles and cartridges. This applies to all participants.

- You will have a physical exam including height, weight and blood pressure.
- You will be asked about changes in your health since your last visit.
- Your blood sugars will be reviewed and your questions answered
- You will receive refills of your study medication.
- If you are female and you are old enough, a urine pregnancy test will be done.
- A small plastic needle will be inserted in a vein on one of your hands or arms (we call this an IV) for drawing blood samples. This area will be kept warm with a heating pad to improve the blood circulation. If you would like, we will use numbing medicine before placing the IV. An OGTT will be performed exactly as described in visit one. The total amount of blood drawn for this test will be about 8 tablespoons.
- At the end of the test, you will be given lunch.
- You will go home after you have eaten and your blood sugar is stable.

4. Study Visit 4 - 9 months after Visit 1

This visit will be exactly like Visit 2

5. Study Visit 5 – 12 months after Visit 1

This visit will be exactly like Visit 1

- You will return your pill bottles and study medication will be stopped after completion of the final visit.
- You will be asked about any changes to your health and/or medications since your last visit.
- Your blood sugars will be reviewed and any questions answered

6. Study Visit 6 – 15 months after Visit 1

This visit will be exactly like Visit 1

7. Study Visit 7 – 18 months after Visit 1

This visit will be exactly like Visit 2 except that you will not return or receive medications.

8. Study Visit 8 – 21 months after Visit 1

This visit will be exactly like Visit 3

Management of your blood sugars

After each visit the RISE study team will be told if your HbA1c test is within the target range and the study team will discuss this result with you. If your HbA1c was not in the target range, the study team will tell you what to do. For example, if your HbA1c is too high while on study medications, it will be repeated and if it stays too high, you will be scheduled to do Visit 5 early and will then be finished with your involvement in the study.

If your HbA1c stays too high after you have come off study medications (after visit 5), you will have your next scheduled visit as soon as possible and will then be finished with your involvement in the study. After you have finished in RISE, you will return to your primary health provider for further care. We will provide all the information we learned about you during RISE to you and your provider.

Diabetes Related Problems and the Treatment of These Problems

As part of the RISE study visits, we will be testing for other problems sometimes found in people with prediabetes and diabetes. Testing for these problems and treating them is part of caring for children with prediabetes and diabetes. These three problems are:

- high blood pressure,
- protein in the urine (a sign that the diabetes is affecting the kidney)
- high levels of fats (cholesterol or triglycerides).

If we find any of these problems while you are in the RISE study, we will inform you and discuss treatment recommendations with you and your primary health care provider.

Detailed procedure description

Laboratory tests

Blood will be drawn from a vein in your hand or arm to measure how the pancreas produces insulin, diabetes control, and tests for inflammation and blood fat. A urine sample will also be obtained and tested to see how the kidneys are functioning and, if you are female, to be sure that you are not pregnant.

Physical exam

You will have a physical exam done by trained medical staff. This is similar to having a routine doctor's visit and includes measuring your height, weight, heart rate, blood pressure, general physical exam and a puberty exam.

Questionnaires

You will be asked to fill out questionnaires (surveys) about your sleep habits, mood, energy level, and appetite. These questionnaires will take approximately 15 minutes to complete and have been used and validated in previous studies.

Hyperglycemic Clamp

This test will be performed in the Clinical Research Center (CTRC) after you have fasted overnight (nothing to eat or drink from the night before except water). This test will last approximately 3½ hours during which we will increase your blood sugar by infusing sugar water and arginine in the vein, to test how well the pancreas produces insulin. Arginine is an amino acid (protein) that is present in our body and in foods we eat. For this test you will need two IV lines, one for the infusion and the other on the opposite hand or arm to obtain blood every 5-15 minutes to measure blood sugar and hormone levels. Before starting the IV's, we will numb the skin. The hand or arm that is used for blood samples will be kept warm in a heating pad. During this test you will lay in a bed either watching TV or asleep. For the first two and a half hours, we will keep your blood sugar level at approximately 180-200 mg/dl. This level is commonly found in people with mild diabetes after they eat. For the final hour, we will raise your glucose level to approximately 450 mg/dl and then give the arginine. We will collect additional blood samples and end the test. The total amount of blood drawn during the hyperglycemic clamp will be about 15 tablespoons.

At the end of the 3½ hour infusion period, we will stop all the infusions, give you lunch, and watch you for approximately one hour to be sure that you do not develop a temporary low blood sugar level. If your blood sugar starts to decrease too much, we will give you additional glucose by IV or by mouth to prevent a low blood sugar and continue to observe you until your blood sugar levels stabilize. When your blood sugar levels are stable, we will take out the IVs.

Timeline of Study Procedures

Study Visit	**Months after Randomization**	**Procedures**	**Approximate Length of Visit**
Visit 1	0 months (Baseline)	• Height, weight, waist and hip circumference, blood pressure • Medical history • Hyperglycemic clamp • Oral glucose tolerance test (OGTT) • Questionnaires • Collection of DNA, blood and urine for storage * • Blood and urine tests (HbA1c, biomarkers, CBC, blood chemistries, pregnancy test) • Review pill and injection taking • Begin study medications	36 hours (overnight)
Visit 2	3 months	• Medical history	1 hour

		• Weight, blood pressure • Blood and urine tests (HbA1c, pregnancy) • Review pill and injection taking • Give drug supply	
Visit 3	6 months	• Medical history • Weight, blood pressure • Oral glucose tolerance test (OGTT) • Blood and urine tests (HbA1c, biomarkers, CBC, blood chemistries, pregnancy test) • Collection of blood and urine for storage * • Review pill and injection taking • Give drug Supply	4 hours
Visit 4	9 months	• Medical history • Weight, blood pressure • Blood and urine tests (HbA1c, pregnancy test if applicable) • Review pill and injection taking • Give drug supply	1 hour
Visit 5	12 months	• Medical History • Weight, waist and hip circumference, blood pressure • Hyperglycemic clamp • Oral glucose tolerance test (OGTT) • Collection of blood and urine for storage * • Blood and urine tests (HbA1c, biomarkers, CBC, blood chemistries, pregnancy) • Collect pills and injections. • Discontinue study medications	36 hours (overnight)
Visit 6	15 months	• Weight, waist and hip circumference, blood pressure • Hyperglycemic clamp • Oral glucose tolerance test (OGTT) • Collection of blood and urine for storage * • Blood and urine tests (HbA1c, biomarkers, pregnancy test)	36 hours (overnight)
Visit 7	18 months	• Medical history	1 hour

		• Weight, blood pressure • Blood and urine tests (HbA1c, pregnancy test if applicable)	
Visit 8	21 months	• Medical history • Weight, blood pressure • Oral glucose tolerance test (OGTT) • Blood and urine tests (HbA1c, biomarkers, CBC, blood chemistries, pregnancy test) • Collection of blood and urine for storage *	4 hours

***** Only collected if consent is given for these procedures.

What are the possible discomforts or risks?

Risk of Feeling Uncomfortable: Even when there is no ill intention on the part of the person asking questions, some people become embarrassed when asked detailed questions. Some people get upset when they have a physical examination. You do not have to do anything that upsets you or makes you uncomfortable.

Risk of Drawing Blood: There is minor risk of infection associated with having your blood drawn. A child may faint or become sick to the stomach at the sight of a needle or when blood is drawn. There can be some discomfort or bruising at the site of the blood draw, but it will go away within a few days.

Risk of Drinking Sugar Water: About one out of ten people have mild nausea or an upset stomach with the glucose (sugar) drink that is given during the oral glucose test. Rarely some people may experience a mild low blood sugar reaction (symptoms like nervousness or sweating) at the end of the test. You will be given a snack to guard against this.
Increasing the blood sugar level rapidly may cause a warm sensation all over, lasting a few seconds. Very occasionally, a vein will become irritated or inflamed (about 1%–2% of the time) after a glucose injection. This problem is treated with Tylenol or ibuprofen and goes away on its own over a few days.

Risk of Giving Arginine by IV: This can cause flushing, nausea, vomiting, headache, and allergic reaction. As with other IV solutions, it can cause irritation of the vein and surrounding tissues which will be reduced by using a large vein for infusion.

Risks Associated with Metformin

The FDA has approved metformin for treating diabetes in adults and children but not in prediabetes. We obtained special permission from the FDA to use metformin for this protocol. There are risks associated with metformin that you should be aware of. If you have kidney or liver problems or if you are allergic to metformin, you should inform the RISE study doctor. You should talk to the study doctor before you undergo any surgery

or undergo any x-ray procedures that use any type of injection of contrast (such as a dye to make the x-ray easier to see). We strongly discourage the use of alcohol in all teenagers. In addition, alcohol should not be used while taking metformin.

The most common side effects from metformin include nausea, diarrhea, vomiting, bloating, excessive gas, loss of appetite, and an unpleasant taste in the mouth. These are more common when the drug is first started and often disappear over time. About 30% (30 out of 100 people) experience symptoms. Other effects include lower than normal vitamin B12 levels in the blood which can lead to anemia (low blood count), hypoglycemia (low blood sugar) when metformin is taken with other diabetes medicines.

In rare instances (3 in 100,000 people), a condition called lactic acidosis has been reported in patients using metformin. It is usually associated with certain medical or surgical problems (including those given above). You must notify your RISE study doctor if you experience a general feeling of uneasiness or discomfort, muscle tenderness or pain, breathing problems, unusual sleepiness or stomach discomfort, or any other unexplained symptom(s). Other signs may be low body temperature (hypothermia), decreased blood pressure (hypotension), and a slowed heartbeat (bradycardia). If ignored or untreated, lactic acidosis can lead to serious effects progressing to coma or death.

Risks Associated with Insulin Glargine

The FDA has approved insulin glargine for treating type 2 diabetes in adults and type 1 diabetes in children. We obtained special permission from the Food and Drug Administration to use glargine in this study. The side effects of insulin glargine include hypoglycemia (low blood sugar) and slight weight gain. If you are assigned to take insulin glargine you will be counseled about the possibility of weight gain while on insulin therapy and given dietary counseling and resources. You will also perform self-monitoring of blood glucose to minimize the risk of low blood sugar.

The symptoms of low blood sugar include feeling hungry, tired, nervous, shaky, sweaty, nauseated, confused, or having a rapid heartbeat or personality changes. If a person drinks or eats sugar-containing food right away, the symptoms will usually stop. In the most severe cases, low blood sugar can cause unconsciousness and seizures. If you have these symptoms, you will need to check your blood sugar to be sure that these feelings are actually caused by low sugar. As part of the education, we will teach you about the signs and symptoms of low blood sugar and what to do.

Risks of Stopping, Starting, or Changing Medications

Any time that a diabetes medication is started, stopped, or changed, there is a risk that you may have more high sugars (hyperglycemia) or low sugars (hypoglycemia as described above).

The symptoms of high blood sugar include drowsiness, thirst, excessive urination, blurry vision, and loss of appetite. If you begin to go to the bathroom much more often or start

wetting the bed after the medicine is changed, you will need to check your blood sugar more often and also check the urine for ketones. As part of the education we will teach you about the signs and symptoms of high blood sugar and what to do. It is important that you call RISE study staff whenever you suspect you have high blood sugar levels.

Risks if You Become Pregnant

Effects of the study medicines on how an unborn baby grows and develops are not known. Birth defects, including physical deformities, mental retardation, premature birth, or other problems, are known risks of some drugs. Because we do not know the effects of the RISE medicines on a baby before it is born, it is important that you not become pregnant during the study. However, metformin and insulin glargine are often used during pregnancy; therefore it is very unlikely to harm a fetus. In addition, the study medications may improve the health of a woman's ovaries, and increase the likelihood of getting pregnant. Therefore, it is very important for girls in the study to avoid getting pregnant.

Teenage girls have the legal right to keep birth control and pregnancy information private, even from their parents. All girls in the RISE study will receive private birth control counseling. For teenagers, we strongly encourage abstinence. However, if you say that you are going to be sexually active or there is any chance that you could become pregnant, you must use one of the allowed birth control methods for at least 1 month before screening, for the entire time that you are in the RISE study, and for at least 30 days after the RISE study is over. This is required by the RISE study. The RISE study doctor or nurse can explain the allowed birth control methods and help you decide which might be best for you. The study doctor can also suggest where you can get more information and advice. We will not tell parents whether their daughter is on any type of birth control unless she gives us permission.

We will do a pregnancy test at every study visit. If you suspect that you are pregnant or are concerned that you may have become pregnant, you should advise the RISE study doctor immediately. If you become pregnant during the treatment phase of the RISE study, you will be withdrawn from the study. We will refer you for medical care to a doctor who specializes in taking care of pregnant women who have diabetes.

Unforeseen Risks

The study may include risks that are unknown at this time. Your participation may be ended if any adverse reactions occur.

What are the possible benefits of the study?

This study is being done to see if medications used for the treatment of type 2 diabetes can help the body to make insulin or slow the progression of prediabetes or early type 2 diabetes in teenagers. There is no guarantee your health will improve by participating in this study. Also, there may be risks, as discussed in the section describing discomforts or risks.

Alternative Treatments

The alternative treatment for type 2 diabetes is the standard of care, which includes metformin, insulin and daily blood sugar testing. The alternative treatment for prediabetes is diet and exercise.

Who is paying for this study?

National Institute of Diabetes, Digestive Disease and Kidney (NIDDK).

Will I be paid for being in the study?

We know that RISE study activities require a lot of effort on your part. Because of this, we will pay you $xx for visits 2, 4, and 7; $xx for visits 3 and 8; $xx for visit 1; $xx for visit 5; and $xx for visit 6. This is a total of $xx if you complete all of the study visits. It is important to know that payment for participation in a study is taxable income.

We will also pay you back for costs related to getting to your study visits. For example, we will be able to pay for the costs of parking or bus fare. Please feel free to discuss this with the RISE staff.

Will I have to pay for anything?

It will not cost you anything to be in the study.

Is my participation voluntary?

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

Can I be removed from this study?

The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, if you become pregnant, or for any other reason. Also, the sponsor may stop the study at any time.

What happens if I am injured or hurt during the study?

If you have an injury while you are in this study, you should call Dr. xxx immediately. Her phone number is xx. We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?

The researcher carrying out this study is xxx, MD. You may ask any questions you have now. If you have questions later, you may call the research coordinator xxx, at xxx. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call xxx, Research Coordinator, with questions. You can also call the Institutional Review Board at xxx.

You can also talk to a Subject Advocate at the Clinical and Translational Research Center (CTRC). The phone number there is xxx.

Who will see my research information?

The xxx and the hospital(s) it works with have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include:

- xxx
- xxx

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

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

We will do everything we can to keep your records a secret. It cannot be guaranteed.

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

xxx

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

- Federal offices such as the Food and Drug Administration (FDA) that protect research subjects like you.

- People at the Institutional Review Board
- The study doctor and the rest of the study team.
- NIH/NIDDK, who is the company paying for this research study.
- Officials at the institution where the research is being conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research

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

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

We respect your right to privacy. But there are some things we cannot keep private. If you give us information about child neglect or abuse, we have to report that to Social Services. If you give us information about someone hurting someone else, we have to report that to the police.

To help us further protect your privacy, the investigators have obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS).

With this Certificate, the investigators cannot be forced (for example by court subpoena) to disclose research information that may identify you in any Federal, State, or local civil, criminal, administrative, legislative, or other proceedings. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

You should understand that a Confidentiality Certificate does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. Note however, that if an insurer or employer learns about your participation, and obtains your consent to receive research information, then the investigator may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

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

- Name and Demographic Information (age, sex, ethnicity, address, phone number, etc.

- Portions of my previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results

- Research Visit and Research Test records

What happens to Data, Blood and Specimens that are collected in this study?

Scientists at the xxx and the hospitals involved in this study work to find the causes and cures of disease. The data, blood and specimens collected from you during this study are important to this study and to future research. If you join this study:

We are asking you (or your child) to provide samples of blood and urine, which will be sent to the NIDDK Central Repositories, a research resource supported by the National Institutes of Health. The Repository collects, stores, and distributes biological samples and associated data from people with many kinds of disorders, from unaffected family members, and from other healthy people. The purpose of this collection is to make samples available for use in research for the study of diabetes, after the current study is completed. Sending samples to the Repository may give scientists valuable research material that can help them to develop new diagnostic tests, new treatments, and new ways to prevent diseases.

The Repository will take measures to protect your privacy, although no guarantee of confidentiality can be absolute. Before the researchers in this study send samples to the Repository, each sample will be given a code number. Your name, or your child's name, and all personal identifying information, such as address, social security number, and date of birth, will be removed. Therefore, the Repository will not be able to give out your name, or other information that identifies you or your child, to the scientists who receive the samples. However, the Repository and scientists will have some data about you, such as age, sex, diagnosis, race, and outcomes of the initial study.

You will not receive any direct benefit or payment for participating, but your sample may benefit the future health of the community at large or some particular group. Because other researchers will not have access to your identity, neither you nor your physician will get the eventual results of studies that might be performed using your sample. It is possible that data resulting from use of your sample may eventually be used in a research publication. In that event, your name or other identifying information will not be included, as this information will not be available to the researchers.

It is important for you to understand that there is a small chance that some research may yield results that may indirectly have a negative impact on insurability, employability, and/or family relationships of some individuals or groups of people. Sometimes, research results in findings or inventions that have value if they are made or sold. These findings or inventions may be patented or licensed, which could give a company the sole right to make and sell products or offer testing based on the discovery. Some of the profits from this may be paid back to the researchers and the organizations doing this study, but you will not receive any financial benefits.

Your donation is voluntary, and if you choose not to participate there will be no penalty or loss of benefits to which you are entitled.

If you agree to have your sample(s) stored in the Repository, you can change your mind up until the end of the RISE study. When study researchers receive written instructions from you, they will destroy your sample and all information that identifies you. After the RISE study ends, you will not be able to withdraw your sample because the Repository will not know which one is yours. The sample will stay in the Repository indefinitely.

Additional Information Resulting From Trial

You will be notified of any significant findings that develop during the course of the research study which may affect your ability or willingness to continue participation in this study.

Additionally, a summary of the research results may be available to you after the results have been analyzed. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Agreement to be in this study

I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I know that being in this study is voluntary. I choose to be in this study. I will get a copy of this consent form.

Signature of Subject:_____ Date:_____
(Age 13 or older)

Print Name:_____

Signature of Parent:_____ Date:_____
(If subject is under age 18)

Print Name:_____

Consent form explained by:_____ Date:_____

Print Name: _____

Investigator:_____ Date:_____

Witness: _____ Date: _____
(Only if using short form)

Optional Consent for Data and Specimen Banking for Future Research

Dr. xxx would like to keep some of the data and blood that is taken during the study but is not used for other tests. If you agree, the data and samples will be kept and may be used in future research to learn more about diabetes. The research that is done with your data and samples is not designed to specifically help you. It might help people who have diabetes and other diseases in the future. Reports about research done with your data and samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your data and samples will not affect your care.

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

xxxx

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

Sometimes data and samples are used for genetic research (about diseases that are passed on in families). Even if your data and samples are used for this kind of research, the results will not be told to you and will not be put in your health records. Your data and samples will only be used for research and will not be sold. The research done with your data and samples may help to develop new products in the future, but there is no plan for you to be paid.

The possible benefits of research from your data and samples include learning more about what causes diabetes and other diseases, how to prevent them and how to treat them. The greatest risk to you is the release of your private information. Dr. xxx will protect your records so that your name, address and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any data or sample collection and storage by Dr. xxx.

Please read each sentence below and think about your choice. After reading each sentence, circle “yes” or “no.” If you have questions, please talk to your doctor or nurse.

Remember, no matter what you decide to do about the storage and future use of your data and samples, you may still take part in the study.

I give permission for my blood and urine to be stored in a central bank (currently stored at the xxx) for future use by RISE investigators in studies of diabetes, related complications, and heart disease:

_____ YES _____ NO _____ INITIALS

I give permission for my research data to be sent to the NIDDK Central Repository for future use by NIH approved investigators in studies of diabetes, related complications, and heart disease:

_____ YES _____ NO _____ INITIALS

I give permission for my blood and urine to be sent to the NIDDK Central Repository for future use by NIH approved investigators in studies of diabetes, related complications, and heart disease:

_____ YES _____ NO _____ INITIALS

Permission to store genetic information (DNA)

If you do agree to having a sample for DNA collected, then in the future, investigators may perform DNA analysis on your blood sample to help better understand diabetes, metabolic disorders, obesity, or other health problems. You will not be notified of the purpose of these studies. This research may include technology or techniques that are not known today. Upon doing this the researchers may discover that you have a risk factor for a specific disease(s) or abnormal chromosome pattern. You usually will not be told of the results, however, in rare cases, if the researchers do find something wrong that can make a significant difference in your life, then attempts may be made to contact you with the results.

I give permission for my blood to be sent to the NIDDK Central Repository for future use by NIH approved investigators in DNA studies.

_____ YES _____ NO _____ INITIALS

Permission to be re-contacted for future studies

It is possible that future studies will come as a result of the findings from the RISE study. If you agree to be re-contacted, we will store your contact information in a locked file in a secure place and if such studies arise in the future, we may re-contact you to see if you are interested in such studies.

Consent Form Approval

I give permission to be re-contacted by the investigators of this study regarding future studies of diabetes, related complications, and heart disease:

_____ YES _____ NO _____ INITIALS

I have read this description about the storage of my data and specimens or it was read to me. I understand the possible risks and benefits of this storage. I agree to take part in the storage and future research use of my data and blood as indicated above.

Signature_____ Date_____