Informed Consent Form
For Parent/Legal Guardian
and Participants Reaching the Age of Majority

Sponsor / Study Title:	**Eli Lilly and Company / "A Prospective, Randomized, Double-Blind Comparison of LY900014 to Humalog with an Open-Label Postprandial LY900014 Treatment Group in Children and Adolescents with Type 1 Diabetes (PRONTO-Peds)"**
Protocol Number:	**I8B-MC-ITSB(a)**
Principal Investigator: (Study Doctor)	**Anuj Bhargava, M.D.**
Telephone:	**(515) 329-6800 (24 Hours)**
Address:	**Iowa Diabetes and Endocrinology Research Center 1031 Office Park Rd, Suite 2 West Des Moines, IA 50265**

If you are the parent or legal guardian of a child who may take part in this study, your permission and the permission of your child (for children 7 years and older) will be needed. When "you" appears in this form, it refers to your child except where it says otherwise.

Introduction

You are being asked to voluntarily be in a medical research study of a study drug known as LY900014. Eli Lilly and Company, and its representatives ("sponsor"), is sponsoring this study and are paying the study doctor and/or the study site for their work in this study.

The purpose of this form is to help you decide if you want to be in this study.

Please read this form carefully. It may contain words that you do not understand. Please ask the study doctor or study nurse to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this form to think about or discuss with family or friends before making your decision. If you sign and date this form, you are giving your permission (or consent) to be a part of this study. You can agree to take part in this study and change your mind later.

An investigator on this study is being paid by Eli Lilly and Company, the company sponsoring this research study, for activities that are not part of the study. These activities may include, for instance, consulting, serving on advisory boards, or giving speeches. Please speak with your study doctor if you have questions about this.

If any important new information is found during this study that may affect your wanting to continue to be part of this study, you will be told about it right away.

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.

Why is this study being done?

The study drug for this research study is called LY900014. It is a type of mealtime insulin. The main reason for you to take part in this study is to help in answering the following research questions:

- Does LY900014 help to lower blood glucose levels in patients with type 1 diabetes?
- How LY900014 controls blood glucose levels compared to Humalog.

"Investigational" means that the drug being tested has not been approved for routine clinical use or for the use described in this study by the United States Food and Drug Administration (FDA). The FDA is allowing the use of this drug for research.

How many people will take part in the study?

Approximately 708 study participants will be taking part in this study.

What will happen during the study?

You will be asked to:

- Sign and date this consent form
- Give your health history. The study staff will review your medical history and test results to see if you can be part of this study
- Tell the study staff if you take any over-the-counter or prescription drugs, vitamins, or herbs

The study staff will discuss what is required for you to be part of this study.

You may not take part in this study if:

- You have had more than 1 emergency treatment for very low blood glucose or poor blood glucose control in the last 6 months
- You are currently receiving dialysis
- You have a history of renal impairment (kidney problems) or a renal (kidney) transplant
- You have had, or are now being treated for, certain types of cancer
- You have major problems with your heart, kidneys, liver, or you have a blood disorder
- You are allergic to Humalog or LY900014.

You may need to have some exams or tests done to find out if you are a candidate to begin the study drug. Some of these tests may be done, even if you do not join the study, as part of your normal care.

This study is divided into different parts, including: screening period, lead in period, study treatment period, and follow-up period.

Screening Period (1 week): The study doctor or clinical staff will talk to you and let you know if you can take part in this study.

Lead In Period (4 weeks): During this period, you will continue treatment with your long-acting insulin.

If you are not already taking Humalog, you will be switched to Humalog as your mealtime insulin. You will also be trained on study procedures including completion of your paper study diary and how to use the study glucometer.

Study Treatment Period (26 weeks): In this study, 3 different mealtime insulin treatment regimens are being studied:

- Study Treatments A and B: You will be asked to inject LY900014 or Humalog within 0 to 2 minutes before each meal for a period of 26 weeks. Neither you nor the study doctor will know which study treatment you are taking.
- Study Treatment C: You will be asked to inject LY900014 up to 20 minutes after the start of a meal for 26 weeks.

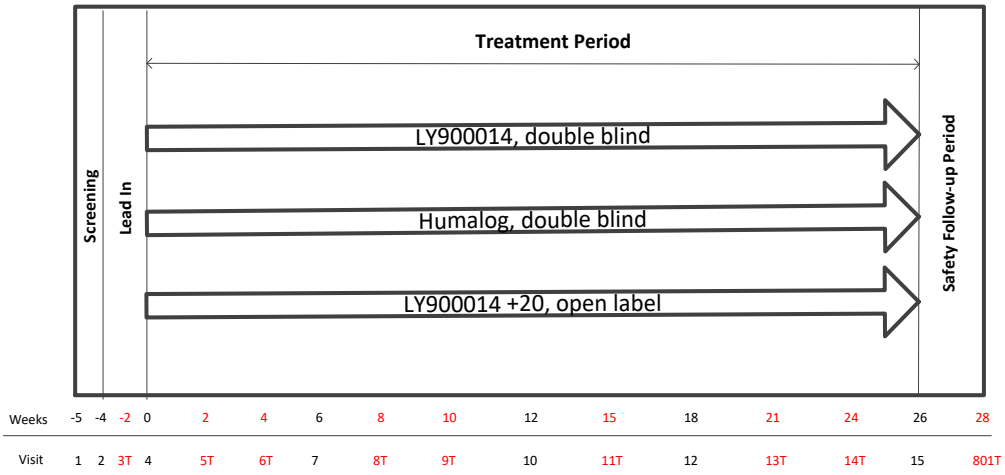
Follow-Up Period (2 weeks): This is a safety follow-up.

Whether you receive study treatment regimen A, B, or C will be determined by chance. The chance that you get the mealtime insulin treatment A, B, or C is 2:2:1. You will use prefilled insulin pens for injection of study insulin. The study staff will provide instructions for injection of study insulin.

You must be taking one of the allowed long-acting insulins in this study which are insulin glargine, insulin detemir, or insulin degludec.

Your study doctor may adjust your mealtime insulin and long-acting insulin doses depending on how your body responds to the study insulin so you reach your target blood glucose levels.

Follow-Up Period (2 weeks): Upon completion of the study treatment period, your study doctor will discuss the insulin treatment options available to you. Your health will be monitored for about 2 weeks. If you discontinue study participation earlier than planned, your health will still be monitored for about 2 weeks.



T=telephone visit

You will:

- Use the study drug only as instructed by the study staff;
- Return any unused study drug and containers at the end of this study, or as instructed by the study staff;
- Use a paper study diary as instructed by the study staff. You will use the diary to record blood glucose results, low blood glucose information, and insulin doses. If you wear a personal CGM/FGM device, you can also print out or download the information.
- Bring the completed paper study diary and study blood glucose meter or your personal CGM/FGM to each study office visit to discuss the results. During the telephone visits, you should also have the paper study diary available to discuss entries with the study doctor or study nurse.
- On certain days before some visits, you will need to check your blood glucose 7 times in a 1-day period. On these days, you should eat a morning, midday, and evening meal.
    - You must use the study glucose meter for these glucose measurements even if you wear a CGM/FGM device.

Your participation in the study is important to find out how well the insulin works to manage your type 1 diabetes, and will be combined with information from other participants. Your participation and completion of study visits and tests is important even if you stop the study treatment. You should not donate blood or blood products during the study.

It is important that you are completely truthful with the study staff about your health history. You should not take part in this study if you do not meet all requirements.

If you choose to be in this study, your part in the study is expected to last up to about 33 weeks.

Please review the table below. This will give you information about what will happen at each specific visit and how often the procedures will happen.

Attachment 1: Study Schedule of ITSB

	Study Screening	Lead-In		On the Study Drug												Safety Follow-Up	ED	Notes
Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**801**		
Study Weeks				**0**	**2**	**4**	**6**	**8**	**10**	**12**	**15**	**18**	**21**	**24**	**26**	**28**		
Phone visits (grey shaded)			**X**		**X**	**X**		**X**	**X**		**X**		**X**	**X**		**X**		
Procedures:																		
Sign informed consent.	X																	
Medical history.	X																	
Physical exam (focused).	X	X		X			X			X		X			X		X	
Weight, blood pressure, and pulse are measured.	X*	X		X*			X			X*		X			X*		X*	*Height is also measured.
Provide site staff with the names of the medications you are currently taking.	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Tell site staff about any new medical problems, symptoms, or issues with the study insulin used in the study.		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	
Receive diabetes and nutrition counselling.		X																
Your study doctor will review your long-acting and mealtime insulin doses and make changes as needed.		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

	Study Screening	**Lead-In**		**On the Study Drug**												**Safety Follow-Up**	**ED**	**Notes**
Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**801**		
Study Weeks				**0**	**2**	**4**	**6**	**8**	**10**	**12**	**15**	**18**	**21**	**24**	**26**	**28**		
Phone visits (grey shaded)			**X**		**X**	**X**		**X**	**X**		**X**		**X**	**X**		**X**		
You will receive a paper study diary and bring it to the site with you.		X		X			X			X		X			X		X	
You will receive a blood glucose meter and supplies andwill be trained on how to use the blood glucose meter.		X		X			X			X		X						
You will be trained on when to collect 4- and 7-point glucoses and how to complete all entries in the study diary, including hypoglycemia information. *		X																You may be given additional training, if needed. *If you wear a personal CGM/FGM, you will not need to use the study glucose meter for the 4-point measurements.
Your study doctor or study nurse will review and discuss SMBG, CGM/FGM results and hypoglycemia from your study diary with you.			X	X	X	X	X	X	X	X	X	X	X	X	X	X		You will need to record the glucose values in your diary or print out or download from your personal device.
Receive study drug.		X		X			X			X		X						
Return unused study drug supplies.				X			X			X		X			X		X	
Pregnancy test for women who could become pregnant.	X			X														By a blood test at Visit 1. By a urine test at Visit 4.

	Study Screening	**Lead-In**		**On the Study Drug**												**Safety Follow-Up**	**ED**	**Notes**
Visit Number	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**801**		
Study Weeks				**0**	**2**	**4**	**6**	**8**	**10**	**12**	**15**	**18**	**21**	**24**	**26**	**28**		
Phone visits (grey shaded)			**X**		**X**	**X**		**X**	**X**		**X**		**X**	**X**		**X**		
Have blood drawn — approximate amount in mL (and tsp).	10 (2)			6.5 (1)			6.5 (1)			6.5 (1)					10 (2)		10 (2)	Additional blood may be drawn for safety reasons.

Abbreviations: CGM = continuous glucose monitor; ED = early discontinuation; FGM = flash glucose monitor; SMBG = self-monitored blood glucose; tsp=teaspoon

Are samples being collected?

Please review the information below. This explains what samples are being collected, how they will be used, and how long they will be stored. Additional samples may be required to repeat a test if needed. The samples and any data generated from the sample can only be linked back to the study participant by the study staff at the site.

General Information Regarding Sample Collection

Various blood samples will be collected from you during this study. The specific procedures for collecting these samples and the risks associated with collection are explained in the procedure table and risks section in this document. Your samples will be identified by your study participant number, and not by your name.

The analysis of your sample(s) may contribute to the creation of new laboratory tests, new medicines, or other items that may be commercially valuable to the sponsor. The sponsor has no plans to provide you, either now or in the future, any compensation, royalty, or any other financial benefit that might result from any product, procedure, or other item that may be developed from studying your sample(s) or any information or data that is derived from such research

Samples for Study Qualification and Health Monitoring

Blood and urine samples will be collected to determine if you meet the requirements to participate in this study.

Additional blood samples and urine samples will be collected throughout the study to monitor your health and your response to study drug.

If some of your blood tests are high, additional blood samples may be tested for hepatitis A, B, C, and/or E, which are serious and contagious diseases. If your test results are positive, your study doctor or staff will contact you. The results of hepatitis A, B, C, and/or E testing will be kept confidential and disclosed only as required by law. Positive test results may be required by law to be reported to local health authorities.

All samples collected for Study Qualification and Health Monitoring will be destroyed within 60 days of confirmation of the test results, unless laws, regulations, or international laboratory certification standards require a longer retention period. This confirmation will either occur immediately after initial testing, or may require that samples be held to be retested at a defined later point in time.

Samples for Antibody Research

Blood sample(s) will be collected to determine if your body produces antibodies against the study drug. Antibodies may affect how a drug works in your body if you take it in the future. The sample(s) may be stored for up to 15 years after this study is finished.

What will happen when I am finished with the study?

After completion of study treatment (Visit 15 or early discontinuation [ED]), it is recommended that participants return to their prestudy mealtime insulin; however, the choice of insulin therapy should be made by the study doctor in consultation with the participant or caregiver.

What side effects or risks can I expect from being in the study?

There may be risks to you if you are in this study. Lilly regularly reviews all important safety information for their study drugs.

As of 30 April 2019, in the completed and ongoing studies, approximately 2111 healthy participants and participants with diabetes have received LY900014.

As of 30 April 2018, cumulative patient exposure of Lilly's Humalog products totaled approximately 92.1 million patient-years.

Like other insulin products, the most common risk with LY900014 or Humalog is low blood glucose, which could cause lack of energy, hunger, confusion, pounding heart, sweating, shakiness, and headache. Low blood glucose may occur overnight. Participants may also have a blood glucose low enough that they cannot treat themselves. Severe cases of low blood glucose could cause seizures, unconsciousness and, in extreme cases, death.

The risk of low blood glucose after taking Humalog can be lowered if you eat food within 15 minutes of injecting your insulin and if you do not do heavy exercise for 2 hours after your injection.

Occasionally, participants taking any insulin, including LY900014 or Humalog, may experience weight gain, swelling due to fluid retention, or pain, redness, swelling, or itching where the insulin is injected. Rarely, a dimple or depression in the skin or an enlargement or thickening of the tissue under the skin may form over time if the insulin, including LY900014 or Humalog, is always injected in the same place. Participants taking any insulin, including LY900014 or Humalog, may experience a generalized allergic reaction, a very rare but possibly life-threatening event.

Read the Instructions for Use provided before using the KwikPen® insulin pen, insulin pump, or vial and syringe.

During the study, LY900014 and insulin Humalog will be provided as prefilled pens for injection.

You must read the entire "Instructions For Use" before using the pen and must carefully follow the directions. If you do not follow the directions provided with the pen or if you use the pen incorrectly, you may receive too much or too little insulin. This may result in either low or high blood glucose. If any part of the pen looks like it is damaged or broken, you should not use the pen and should return it to your study doctor. A pen that does not work properly may deliver too much or too little insulin even if the directions are followed exactly.

Procedure Risks

Please talk to the study doctor or staff about any questions or concerns that you may have about the procedures required for this study.

Glucose Monitoring:

You will be expected to check your blood glucose at least 4 times per day during the study, and, sometimes, up to 7 times in a 1-day period. If you wear a personal continuous glucose monitor

(CGM)/flash glucose monitor (FGM) that allows you to use results for insulin dosing, you will only need to use the study glucose meter for the 7-point blood glucose measurements. Blood glucose testing requires pricking your finger or other area as directed by the study staff and testing a drop of blood. This does not usually cause serious problems, but it can cause some discomfort. The risks would be similar to those described for blood tests and injections.

Risks of Subcutaneous (SC) Injection:

For most people, needle punctures for SC shots do not cause any serious problems. Sometimes they may cause bleeding or bruising where the shot is given. Sometimes people complain of discomfort, infections, and/or pain at the site of the shot. Infection may happen with SC shots because the needle breaks the skin. Then germs can get into the skin underneath. Shots may cause abscesses or skin and soft tissue infections. Additionally, if a blood vessel is hit by the needle, the risk of infection will be even greater if germs are taken into the blood system.

Allergic Reaction or Antibodies to Insulin Injections:

Your body's immune system may react to any insulin, including LY900014, by making proteins (antibodies) that attack objects that enter the body. These proteins that form against insulin could cause an allergic reaction. It could also interfere with how your body normally reacts to insulin. This could lead to low or high blood glucose, which would require insulin dose adjustments. Blood samples will be taken to see if your body is forming insulin antibodies. Rarely, some people can have a whole-body allergic reaction which may be life-threatening.

Risks of Blood Tests:

For most people, needle punctures for blood draws do not cause any bad problems. However, sometimes they may cause bleeding, bruising, discomfort, infections, and/or pain where you had the blood drawn. You may also feel dizzy.

What are the Reproductive Risks?

If you are female, you should not become pregnant or breastfeed a child while in this study. Naturally, the best way to not become pregnant is not to have sex. If you are sexually active, you must use birth control. You should talk with your doctor about the types of birth control that are best for you and your partner. Tell your doctor right away if you become pregnant or think you are pregnant.

Taking part in this study can result in risks to an unborn child or breastfeeding child.

Some methods of birth control may be less effective.

Please discuss birth control methods with your study doctor.

There may also be unknown risks to your embryo, fetus, or nursing child.

If you become pregnant while taking the study drug, you and your newborn will be followed through delivery.

Other Risks

In addition to the side effects already described, LY900014 and other drug(s) required by the protocol, and the study procedures may have other unknown risks.

There may be unknown risks of possible harmful interaction with other medication you may be taking.

You should not give the study drug to other people and should keep it out of the reach of small children.

Are there benefits to taking part in the study?

You may or may not receive any benefit from being in this study. You will receive your basal insulin along with the study drug to treat your diabetes. You may or may not have tighter control of your blood sugars. If you take part in this study, other people with Type 1 diabetes may be helped.

Information obtained from this study will also benefit the sponsor of the study and may benefit study participants in the future. You may receive information from physical examinations, laboratory tests, or other testing that is done in this study but these tests may not have any impact on your health.

What other choices do I have if I do not take part in this study?

You do not have to take part in this study to receive treatment for type 1 diabetes. Other treatments and therapies are available, including the treatments that you are currently using. Your study doctor can discuss this in more detail with you.

What happens if I want to stop the study?

Your taking part in this study is entirely voluntary. You may refuse to take part in the study or you may stop your participation in the study at any time. You may do so without a penalty or loss of benefits to which you are otherwise entitled.

Your participation also may be stopped by the study doctor or sponsor for any reason without your consent. If this happens, it might be due to a bad reaction you have to LY900014 or new information about LY900014 safety or effectiveness.

If you stop being part of this study, the study doctor or one of the staff members will talk to you about any medical issues regarding the stopping of your participation.

What are the costs of taking part in this study?

Study drug and study procedures will be provided at no cost to you. You may have to pay for expenses related to this study such as childcare.

You may have to pay for some expenses related to this study. You will be reimbursed; however, your expenses could be more than the amount you are reimbursed.

Caregiver will receive $50 for visits 1, 2, 4, 7, 10, 12, 15, and/or Early Discontinuation to help reimburse them for their transportation expenses related to your taking part in this study. Depending on how far you travel, you may be eligible for additional reimbursement for excessive mileage expenses you accrued related to your taking part in this study.

Caregiver will receive $50 for visits 1, 2, 4, 7, 10, 12, 15, and/or Early Discontinuation to help reimburse them for their inconvenience of site visits related to your taking part in this study.

Caregiver will receive $25 for visits 3, 5, 6, 8, 9, 11, 13, 14, and 801 to help reimburse them for their inconvenience of telephone visits related to your taking part in this study.

If you do not finish the study, you will be reimbursed for the part of the study that you did complete.

You will be paid following each completed visit.

What happens if I am injured because I took part in this study?

If you are injured, please seek medical help. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured then they will help you get the care you need.

If you follow the directions of the study doctor and staff, the sponsor will pay the medical expenses for the treatment of a physical injury because of a properly given drug or procedures.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

You retain the right to seek compensation for injury even if you sign this form, accept medical care, or accept payment for medical expenses and you retain the right to seek compensation for injury related to the negligence of those involved in the research.

Who should I contact if there is an emergency or if I have questions?

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00031112.

Will my medical information be kept private?

The study doctor and staff will handle your personal health information in a confidential manner.

By signing the consent document for this study, you give permission ("authorization") for the uses and disclosures of your personal health information in the following ways.

- Your original medical records (which may contain your full name or other information that may directly identify you) may be shared with or viewed by to ensure the quality of the study conduct and study data:
  - The sponsor of the study and its representatives "sponsor",
  - the regulatory authorities in this country (FDA) and in other countries, and
  - the ethical review board overseeing this study (Advarra IRB).
- Your study data (information collected for the study which only identifies you by a code and not your full name or other information that may directly identify you) may be shared with or viewed by:
  - the sponsor and their business partners (including those in other countries),
    - When the sponsor shares any data outside of this country, the sponsor will respect the terms of this data privacy statement even if other countries may have privacy laws that do not provide the same protections
    - The sponsor will only share your study data with their business partners, only if they need the information as a part of this work with the sponsor. The business partners must sign a contract that requires it to protect your study data in the same way as the sponsor.
  - the regulatory authorities in this country (FDA) and in other countries,
  - the ethical review board overseeing this study (Advarra IRB), and
  - the doctors at other institutions participating in the study.
- The sponsor will use the study data:
  - to support the study purposes described in the consent document,
  - to determine how safe or effective any of the drugs or treatments included in the study,
  - to better understand the disease(s) included in the study, or
  - to improve the design of future studies.

- Study data that does not directly identify you may be published.

Your personal health information may no longer be protected under the HIPAA privacy rule once it is disclosed by your study doctor to these other parties.

You have the right to see and copy your personal health information related to the research study. However, you may not be able to review some of the study data until after the study has been completed to ensure the scientific integrity of the study.

Your authorization for the uses and disclosures of your personal health information does not have an expiration date. In California and any other state that requires an expiration date, the Authorization will expire 50 years after you sign this authorization document.

You may cancel your authorization for the uses and disclosures of your personal health information at any time by providing written notice to the study doctor at the address listed on page one of this consent form. If you cancel your authorization:

- The study doctor and staff will only use or disclose some of your personal health information if it is needed to confirm the accuracy of the study data.
- The sponsor will still use study data that was collected before you cancelled your authorization.
- You will no longer be able to participate in the study.

_____

Printed Name of Subject

_____ _____

Signature of Subject (if age of majority or older) Date

_____

Printed Name of Parent/Legal Guardian
(if participant is under age of majority)

_____ _____

Signature of Parent/Legal Guardian Date
(if participant is under age of majority)

Study Participant Information and Consent Form Signature Page

To become a part of this study, and to authorize use and disclosure of your personal health information, you must sign and date this page.

Only sign this consent after:

- You have read all of the information in this Study Participant Information and Consent Form, and you have had time to think about it.
- All of your questions have been answered to your satisfaction.

You voluntarily agree to be part of this research study, and to do the following:

- to follow the study procedures,
- to provide necessary information to the study doctor, nurses, or other staff members, as requested, and
- allow the study doctor and the sponsor to use and disclose your personal health information as described in this document

You may freely choose to stop being a part of this study at any time. You will receive a copy of this signed and dated Study Participant Information and Consent Form to keep.

FOR ADULT STUDY PARTICIPANT TO COMPLETE
Applicable for Study Participant who turns 18 during this study.

Signature of Adult Study Participant	Date (Adult Study Participant must personally date)
Adult Study Participant Name (print or type)	

FOR PARENT/LEGAL GUARDIAN TO COMPLETE

Applicable only when persons other than the study participant are authorized under local law to consent on behalf of the study participant in order for the study participant to participate in the study.

Signature of Parent/Legal Guardian	Date (Legal Representative must personally date)

Parent/Legal Guardian Name (print or type)

If signed by legal guardian, state description of relationship to study participant or other basis for legal authority

FOR INDIVIDUAL CONDUCTING INFORMED CONSENT DISCUSSION TO COMPLETE

I have explained the study (such as the purpose, risks, benefits and the procedures) to the study participant and the participant's parent/legal guardian before the study participant voluntarily agreed to participate.

Name of Individual Conducting Informed Consent Discussion (print or type)

Signature of Individual Conducting Informed Consent Discussion	Date (Individual Conducting Informed Consent Discussion must personally date)