Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____ **Medical Record #** _____

Principal Investigator: Sue Brown, M.D.
University of Virginia
Department of Endocrinology & Metabolism
Box 801405 Charlottesville, VA 22908

Sponsor: National Institute of Health (NIH)

What is the purpose of this form?

This form will help you decide if you want to be in the research study. You need to be informed about the study, before you can decide if you want to be in it. You do not have to be in the study if you do not want to. You should have all your questions answered before you give your permission or consent to be in the study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will get a copy of this signed form.

Who is funding this study?

This study is paid for by a grant from the National Institute of Health (NIH). The insulin pump will be provided by Roche Diagnostics Corporation. One Touch Blood Glucose Meters (Lifescan Corp.) and continuous glucose monitor supplies (DexCom Corporation) may be purchased with grant funding.

Why is this research being done?

The purpose of this study is to see if an investigational type of technology that helps control blood sugar in people with type 1 diabetes mellitus who are on insulin pump therapy, can successfully be used and supervised in a non-hospital (research house) setting. This system is called the Advisory/Automated Adaptive (AAA) Control system.

In individuals with type 1 diabetes mellitus (T1DM), the immune system destroys pancreatic cells and the body cannot make insulin to control the blood sugar. Patients on insulin pumps have insulin administered through a cannula (plastic tubing) under the skin both continuously as a basal rate and as boluses based on the amount of carbohydrates in a meal (carb ratio). Basal rates and boluses are given to correct the blood sugar if it is not at

the target level (correction factor). Some of the challenges of insulin treatment are keeping the blood sugar from getting too high after a meal and preventing low blood sugars.

What is an Artificial Pancreas?

The artificial pancreas (AP), known as Closed-Loop Control of blood glucose in diabetes, is a system combining a continuous glucose monitor (glucose sensor), a control algorithm (complex mathematical formulas), and an insulin pump. The algorithms are intended to maintain your blood glucose level within a certain range. This is called Control-to-Range.

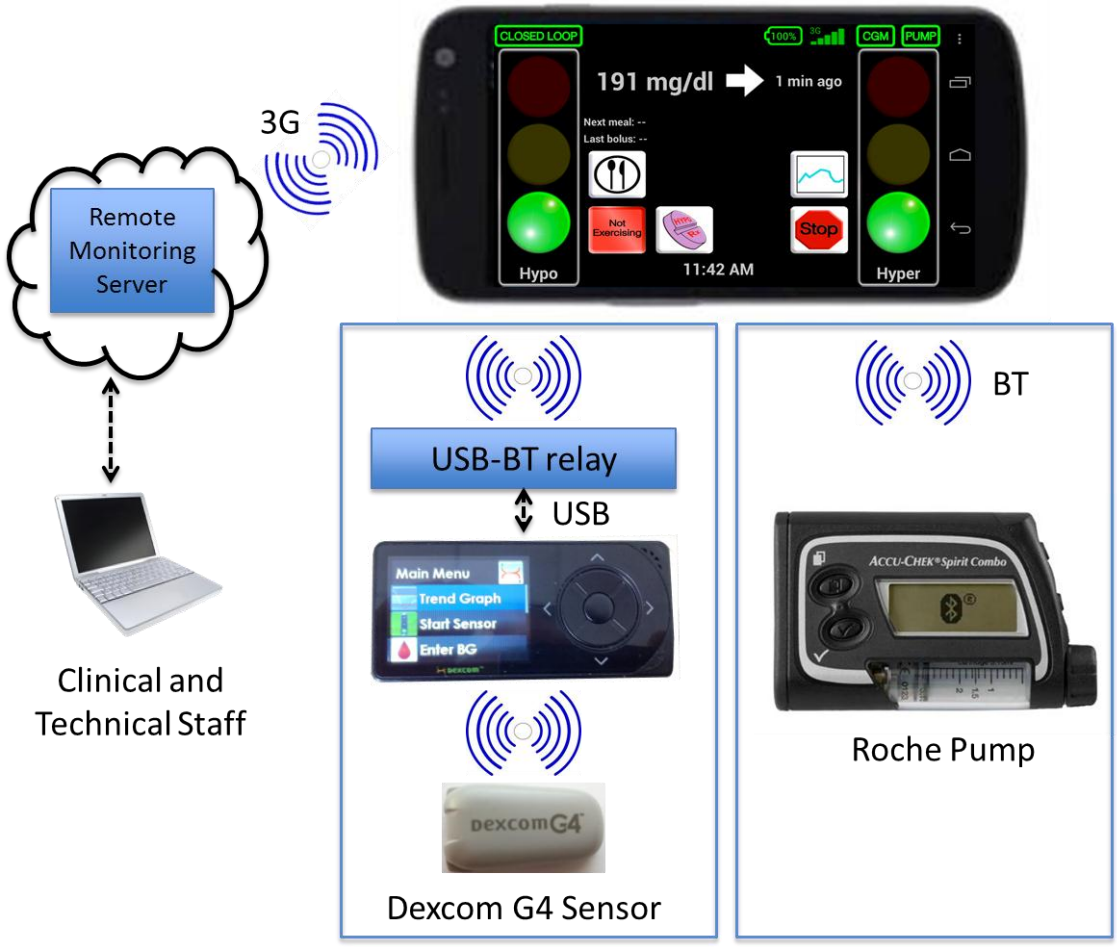

Figure 1: DiAs Medical Platform System Components

You will learn how to operate the **DiAs (Diabetes Assistant) Medical Platform System.** The **DiAs** includes:

1. **DiAs** is the central component of our system. It is a standard cell phone running on an Android operating system. The cell phone has been changed to prevent you from (1) using it as a phone or browser, (2) changing the volume (3) accidentally shutting it off. The cell phone runs an algorithm and is connected to work with the insulin pump and continuous glucose monitor to help keep the blood sugar in a desired range and help avoid hypoglycemia during the night.

   DiAs will be connected to the continuous glucose monitor.

   In addition, DiAs will transmit de-identified patient data in real time to a server for remote monitoring. Other study team members will observe the study from their office or home.

2. A **continuous glucose monitoring** device that measures sugar levels in the interstitial fluid in belly fat. Interstitial fluid (or tissue fluid) is a solution that bathes the spaces between the tissue cells. This is different from a finger stick. The continuous glucose monitor device consists of a sensor and a receiver. The sensor has a wire that is inserted just beneath the skin. It measures sugar in the interstitial fluid every 5 minutes. In this study, you will test your blood sugar by taking finger stick blood glucose values.

3. An **insulin pump** adjusts insulin delivery by giving small boluses (small amounts of insulin) every 5 minutes based on interstitial sugar values received from the continuous glucose monitor reading. These readings are then sent to the cell phone. You will use the cell phone to instruct the insulin pump how much insulin to give yourself at meal and correction boluses. The cell phone will also receive updates from the insulin pump.

4. The **algorithm** is a series of complex mathematical equations that advices the system what to do. The algorithms are intended to maintain your blood glucose level within a certain range.

   The Advisory/Automated Adaptive (AAA) Control system, which includes three interacting control modules:
   - **Module 1 –** Automated Safety Supervision Module (SSM) responsible for prevention of hypoglycemia, which can be adapted (individualized) with the data that you collected in the day(s) before the admission;
   - **Module 2 –** Advisory Module (AM) responsible for pre-meal boluses and after-meal corrections, which can be adapted (individualized) with the data that you collected in the day(s) before the admission;
   - **Module 3:** Automated Basal Rate Module (BRM), responsible for adjusting your basal insulin to maintain a certain range as your blood glucose rises and falls particularly during sleep, which can be adapted (individualized) with the data that you collected in the day(s) before the admission.

The Adaptive Advisory/Automated (AAA) system as a whole is not approved by the FDA and is therefore considered investigational. So far, parts of this investigational system combined in different forms has been tested in over 150 people with type 1 diabetes mellitus at UVa and in testing sites in California, Italy and France.

You are being asked to be in this study because:

- You are at least 21 and less than 65 years of age
- You have had Type 1 Diabetes Mellitus for at least 1 year
- You have been using an insulin pump to treat your diabetes for at least 1 year

Up to 45 people will be in this main study at UVa. We will ask 5-8 people who participate in this primary study to participate in a 5 night substudy.

Is there a possible conflict of interest?

When a person or an organization has a financial or other interest large enough to seem as if it could affect their judgment, it is called a conflict of interest. Four study investigators have pending patent applications for the algorithms (complex mathematical equations) in the Adaptive Advisory/Automated (AAA) System. Both the investigators and their institutions may earn financial benefits if this study has positive results.

How long will this study take?

Your participation in this study will require 5 study visits over 9 weeks. The first visit will be a screening visit at the Clinical Research Unit that will last about 2 hours. Visit 2 will be a Study Training session at the Center for Diabetes Technology. The 5 day data collection will begin at the conclusion of this training visit. Visits 3 and 4 are the Experimental and Control Admissions, lasting approximately 40 hours each. The Experimental Admission will take place at a research house located about 3 miles from the University of Virginia Medical Center. The Control Admission may take place in your home.

Up to two people will be asked to enroll for a 24 hour admission prior to the start of the study to ensure system performance.

Five to eight people will be asked to enroll in a substudy in addition to the primary study protocol. Your willingness to participate in the substudy is independent of your participation in the main study.

All procedures outlined in this consent form are being done for research purposes only.

What will happen if you are in the study?

In individuals with type 1 diabetes mellitus (T1DM), the immune system destroys pancreatic cells and the body cannot make insulin to control the blood sugar. Patients on insulin pumps have insulin administered through a

cannula (plastic tubing) under the skin both continuously as a basal rate and as boluses based on the amount of carbohydrates in a meal (carb ratio). Basal rates and boluses are given to correct the blood sugar if it is not at the target level (correction factor). Some of the challenges of insulin treatment are keeping the blood sugar from getting too high after a meal and preventing low blood sugars.

STUDY INTERVENTIONS:

Experimental Admission:
Advisory/Automated Adaptive (AAA) Control with 45 minutes of exercise

Control Admission:
Insulin Pump + Continuous Glucose Monitors with 45 minutes of exercise

You will participate in both the Experimental and the Control Admissions. The order of the two admissions will be randomized (like a flip of a coin). The admissions are exactly the same except for the intervention mode – Closed Loop on the Experimental Admission where you will use the study pump and the continous glucose monitor. A study physician, medically qualified personnel, and a technician will be present with you during the Experimental Admission.

In the Experimental Admission, you control the DiAs with assistance from the study personnel as needed.

During the ***Experimental Admission***, the Advisory/Automated Adaptive system will be tested. The study team will check if DiAs can pick up the information from the continuous glucose monitor and send it to a computer in the next room where medical personnel and a computer technician will be watching it.

- During the daytime (07:00 AM - 11:00 PM) of the Experimental Admission, DiAs will run the Safety System and Advisory Modules.
- During the overnight (11:00 PM - 7:00 AM) of the Experimental Admission, DiAs will run the Safety System and the Basal Rate Modules.

During the ***Control Admission,*** you will use your home insulin pump along with a continuous glucose monitor receiver without running any specialized mathematical equations.

SCREENING (will take about 2 hours to complete):

Visit 1 *(Day 1):*
If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. You will have tests and procedures during this time to make sure you are eligible and it is safe for you to participate. These include the following:

- You will be asked to fill out a medical history form. You will be asked about your diabetes history, past and current medical conditions, surgical history, menstrual history (females), allergies, medications and

supplements, social history (including drinking, smoking and drug habits), and whether or not you have various symptoms. You will also be asked about your pump settings and average daily insulin use over the past 7 days.

- Physical exam and vital signs (blood pressure, heart rate, etc.)
- Height and weight
- Standard blood tests (2 teaspoons of blood) to check certain salts, blood sugar, kidney function, liver function, blood counts, HbA1c (your blood glucose average over 8-12 weeks), Hematocrit (percentage of red blood cells in your blood), and thyroid levels (TSH). This will also include a pregnancy test if you are a woman who can become pregnant. The pregnancy test must be negative in order to participate.
- You may have these blood tests performed locally with any participating LabCorp facility
- You will fill out hypoglycemic treatment preferences.
- You will be asked not to take medications containing acetaminophen (like Tylenol) 24 hours prior to wearing the continuous glucose monitor sensor and while you are wearing the sensor.

If these tests show you are eligible, you will return to the clinic within 8 weeks to begin study procedures.

STUDY TREATMENT

VISIT 2 (Day 2) – Study Training approximately 5-7 days before admission (will take approximately 1-3 hours to complete depending on your knowledge of the continuous glucose monitor):

Equipment Training:

- If you are a woman that can become pregnant, you will have a urine pregnancy test prior to wearing study equipment. The test result must be negative in order to participate in the study.
- Staff will watch you put on one continuous glucose monitor sensor on your abdomen.
- You will be taught how to calibrate the continuous glucose monitors by using the study glucometer and entering the information into the continuous glucose monitors.
- You will be instructed on how to care for the sensor site and how to look for skin irritation after the sensor removal.
- If you are a skilled continuous glucose monitor user prior to the Study Training visit, the study team will review the above related procedures with you, and you may elect to start your continuous glucose monitor at home rather than at the Study Training visit.
- You will perform a self-monitoring blood glucose (also called a finger stick) test with your personal glucometer. You will be instructed that all finger sticks should be preceded by hand washing with warm water and a dry towel. You will be instructed to obtain fingerstick, avoiding alternative sites, when obtaining blood values. The first drop of blood will be discarded. The second hanging drop will be used to measure the glucose level.
- You will be asked to demonstrate proper functioning of your personal glucometer by using control solutions as appropriate for your glucometer.
- The study team will discuss your personal methods of determining carbohydrate counting.

- Instructions will be provided on how to download your insulin pump, continuous glucose monitor and blood glucose meter.
- **You will be asked to complete a minimum of 4 blood glucose fingersticks per day.**
- You can call or visit the study team and study physician as needed. You will be given the telephone numbers of the study team so you call someone 24-hours a day.
- Continuous glucose monitor supplies will be provided to you.
  The study team will discuss your usual meal content, methods for estimating carbohydrates, and your perception of meals that affect your glucose levels.

Things that will occur after this visit:

- You will be asked to calibrate the continuous glucose monitor a minimum of every 12 hours (or as prompted by the continuous glucose monitors device) while at home.
- If a sensor failure occurs, you should replace the sensor with a new one. The study team can assist you with inserting a new sensor if preferred. You should inform the study team of this sensor failure.
- Continuous glucose monitors are intended to provide glucose trend information and are not approved for use as a replacement for fingerstick glucose measurement. ***You should not use information from the continuous glucose monitor to make treatment decisions*** (e.g. take more insulin or treat a low blood sugar). Treatment decisions should only be made based on the results of a fingerstick blood glucose value.
- You will be asked to avoid acetaminophen-containing medications (like Tylenol) while wearing the continuous glucose monitors as any acetaminophen-containing medications may affect the performance of the devices.
- **You will be asked to bring your own insulin for the inpatient admission.**

Data collection (Day 2-7) will include:

- *Continuous Glucose Monitors Data:* The DexCom® stores glucose values every 5 minutes. This data will be uploaded via DexCom Studio software in the data collection system.

- *Fingerstick readings:*
  - You will be asked to perform only fingersticks, with no alternate site testing, for the entirety of the study.
  - You must complete four blood glucose fingerstick readings per day to comply with the requirements for participating in the study. Two of these measurements must be upon waking up and bedtime. Any home blood glucose tests normally done by the participant should continue without interruption.

- *Meal times and Carbohydrate Administration:* You will be asked to use the bolus calculator function of their pump and enter relevant carbohydrate information for meals.

- *Insulin administration*: Information is stored within your insulin pump any time you use the bolus calculator function. This data will be downloaded and sent to the study team the day before their admission. You will be asked to record any additional insulin administration that was not delivered via the insulin pump but was given from an insulin pen or needle injection.

You will be asked to send us the download of your insulin pump data on Day 2 or 3 to ensure the accuracy of the data.

You will be asked to send us the download of this information (insulin pump logs with glucometer information and continuous glucose monitor information) about 1-2 days prior to your admission. The study team will verify that the information is being captured correctly.

You will be asked to insert a second continuous glucose monitor 24-48 hours prior to the Experimental Admission. If you prefer, you may return to the office for study staff to insert the second sensor. This secondary continuous glucose monitor will be used as a back-up continuous glucose monitor during the experimental admission if needed. Insertion of the secondary continuous glucose monitor in advance will allow for appropriate warm-up prior to the Experimental Admission.

While two sensors are operational during the study, only one of them is connected to the DiAs and provides data for the closed loop system. One sensor will be identified as a primary sensor and the other the backup. If either of the continuous glucose monitor devices experiences a sensor failure prior to or during the study, it will be removed and replaced by a new sensor.

You will perform a final upload of continuous glucose monitor, fingersticks and pump information on the evening prior to admission. If you are unable complete the upload, we will ask you to arrive earlier on the day of admission for the study team to download the information. It is possible that this may delay the start of the trial by 1-2 hours. This will allow time for final completion of initialization of the automated advisory system for closed-loop control.

Visit 3 (Day 7-9) *Study Testing (approximately 40 hours):*

TESTING PROCEDURES

RESEARCH HOUSE ADMISSION PROCEDURES

1. You will meet the study team and check in to the research house by approximately 6:00 PM.

2. Your glucose will need to be between 80-249 mg/dL prior to starting Closed Loop Control.
3. You will be asked to perform a fingerstick using the study glucometer shortly after arrival.
4. The study team will confirm that you brought your insulin, insulin pump supplies, and regular medications. The study team will also confirm that you haven't been feeling ill. They will confirm that you haven't taken any acetaminophen (i.e. Tylenol) while wearing the continuous glucose monitor sensor. If all criteria are not met, you will be rescheduled.
5. If you are a woman that can become pregnant, you will have a urine pregnancy test. If positive, you will discontinue study participation. You will be asked to seek confirmation of the test and the appropriate medical care.
6. You will be reminded that all treatment decisions should be based on fingerstick values and not on continuous glucose monitor values.
7. You and the study team will determine which continuous glucose monitor will be the primary sensor.
8. Your preferred hypoglycemia treatment foods (e.g. juice, glucose tablets, milk, etc…) will be available. Study medical personnel will additionally have glucose tablets, glucose gel/liquid, and a glucagon emergency kit available for treatment.
9. You will have access to glucose-free beverages.
10. The study physician will be on site or on-call for any clinical concerns.
11. The senior engineer with remote monitoring capability will view the study from another location. A technician will be on site for system issues.
12. You will be accompanied by a medically qualified staff member and a computer technician during the entire admission.
13. You will be trained on DiAs.

EXPERIMENTAL SCHEDULE:

Day 1 Evening of Admission

1. DiAs will be turned on prior to the evening meal.
2. Dinner will occur at approximately 7:00 PM (between 7:00 – 8:30 PM).
3. Lights will be turned out at approximately 11:00 PM, and you will be encouraged to sleep.
4. A fingerstick value will be obtained at 3:00 AM.

Day 2 of Admission

1. You will be awakened shortly before 7:00 AM and allowed time for routine hygiene.
2. A fingerstick value will be obtained upon waking while you are still fasting.
3. At 7:00 AM, DiAs will detune the Basal Rate Module and activate the Advisory Module. The Advisory Module will be active from 7:00 AM – 11:00 PM.
4. Breakfast will occur approximately 07:00 AM (between 07:00 – 08:30 AM) and insulin administration will occur as described for all meals.

5. Lunch will occur approximately 12:00 PM (between 12:00 PM – 1:00 PM).
6. From 2:00 – 2:45 PM, you will take a walk in the neighborhood or around the grounds of the house. Medical personnel will accompany you, and the system will be observed remotely by the study technician. Staff will carry hypoglycemia treatment supplies, including a glucagon emergency kit.
7. Dinner will occur approximately 7:00 PM (between 7:00 – 8:30 PM).
8. Lights will be turned out at approximately 11:00 PM, and you will be encouraged to sleep.
9. A fingerstick value will be obtained at 3:00 AM.

Day 3 of Admission – Procedures Related To Discharge

1. You will be awakened shortly before 7:00 AM and allowed time for routine hygiene.
2. A fingerstick value will be obtained upon waking while you are still fasting.
3. At 7:00 AM, the DiAs will stop Adaptive Advisory/Automated control. The system components (continuous glucose monitor sensors & study pump) will be removed.
4. You will resume his/her normal home pump therapy.
5. A fingerstick value will be obtained.
6. You will be discharged by approximately 9:00 AM if the following 3 conditions are met:
    a. the fingerstick value is 80-249 mg/dL
    b. the glucose trend is stable
    c. Insulin on Board is appropriate as determined by the study physician

2. If your glucose is out of the specified parameters, the Hypoglycemia or Hyperglycemia Safety Protocol will be followed until it is in the specified range.
3. We will request that you remain at the Research House until approximately 9 AM. During this observational period, we will provide you breakfast.
4. Ketostix may be provided to test ketones should you become hyperglycemic during the next 48 hours.
5. Study staff will contact you within 24-48 hours after discharge.
6. ***If you are participating in the substudy, see Procedures Related to Substudy (page 13).***

Equipment Specifications:

1. All study equipment including the DiAs cell phone, computers, insulin pump, and continuous glucose monitor receivers will use atomic clocks as a reference.
2. DiAs will be initialized with your insulin pump parameters determined from the data collection period and will be connected to the study pump. The study pump will be initiated, and your home pump will be removed.
3. You will be trained to use the DiAs interface. You will be trained how to respond to the Adaptive Advisory/Automated alerts and will be supervised by the study team during the admission.
4. DiAs will be initialized with your insulin pump parameters determined from the data collection period

and will be connected to the study pump. The study pump will be initiated, and your home pump will be removed.

5. You may request advice from the Advisory Module at any time. Advice may be for meal boluses or correction boluses.
6. You must confirm any boluses prior to injection.
7. The Safety Supervision Module and Basal Rate Module will be running throughout the trial. The Safety Supervisory Module is responsible for lowering the basal rate or insulin delivery to avoid hypoglycemia.
8. You will confirm all pre-meal insulin suggested by the DiAs.
9. The Advisory Module, responsible for pre-meal boluses and after-meal corrections. The study team will teach you how to activate the advisory module for advice on pre-meal insulin and anytime that you may need an additional correction following a meal.
10. At 11:00 PM, DiAs will detune the Advisory Module. The Safety Supervision and Basal Rate Modules will be active overnight from 11 PM – 7 AM.
11. The staff will be checking the readings of the secondary receiver at 3:00 AM and 5:00 AM during the night. Additional readings may be taken as necessary.
12. The Advisory Module (AM) will be activated at 7 AM for the remainder of the trial.

Meal Times:

- Breakfast (07:00 – 08:00); Lunch (12:00 – 13:00); Dinner (19:00 – 20:30); optional snack (22:00 – 23:00). You will be permitted to snack between scheduled meals.
- You will not be permitted to snack overnight (11 PM – 7 AM).
- Meal and snack times should be provided at the same time each day between the Experimental and Control Admission.
- Meals and snacks will be prepackaged meals purchased by the study team and will be brought in to the study site.
- Meals and snacks eaten during the Experimental Admission will need to be exactly the same during the control study at home.
- You will determine the carbohydrate estimation for each meal. You will be asked to use the same carbohydrate information for those meals and snacks for insulin dosing.

Meal and Snack Boluses:

- Using the DiAs interface, you will enter carbohydrate amount and fingerstick value;
- The DiAs will recommend bolus treatment;
- You will confirm bolus treatment in the DiAs.
- After you confirm the bolus, the insulin will be injected.

Fingerstick Collection Times:

- Scheduled times: meal time, two hours after a meal 11:00 PM and 3:00 AM
- Prior to any snacks

- Red Light Hypoglycemia Alarm on the DiAs
- Red Light Hyperglycemia Alarm on the DiAs
- CGM alarms more than 260 and will repeat hourly if CGM persistently alarms more than 260
- CGM alarms less than 90 during Experimental Sessions and will repeat hourly if CGM persistently alarms at less than 90
- If the two CGMs differ by more than 20%, a fingerstick will be obtained and calibration performed if equal to or more than 6 hours since last calibration. The frequency of subsequent fingersticks will depend on the actual fingerstick according to Hypoglycemia and Hyperglycemia Safety Protocols. Fingerstick will occur hourly if the CGMs continue to differ by 20%.
- Prior to calibration of CGM
- A subject may request any additional fingersticks as desired
- Study personnel may also request additional fingersticks at their discretion.

PROCEDURES DURING THE CONTROL STUDY AT HOME (DAYS 2-9 or 10-17)

1. You will start a new pump site on the morning of Day 5 or Day 13 (two days before the start of the testing) to avoid initiation of a new site during the Control Study at Home.
2. You will follow the same schedule for timing of meals, snacks, exercise and bedtime as the experimental admission.
3. **On the last two days of the control week (Days 7-9 or 15-17), you will consume the identical meals and snacks as the experimental admission. In the unlikely event, that the identical food is unavailable, the closest match of carbohydrate content will be chosen.**
4. You will administer insulin through your home insulin pump using your usual settings.
5. You will be permitted to use temporary basal rates during this time.

6. You will perform fingersticks using the study glucometer at a minimum at the identical scheduled times as the experimental admission.
7. You will be instructed that all fingersticks should be preceded by hand washing with warm water and a dry towel. You will be instructed to obtain fingerstick, avoiding alternative sites, when obtaining blood values. The first drop of blood will be discarded. The second hanging drop will be used to measure the glucose level.
8. You will be reminded that all treatment decisions should be based on fingerstick values and not on continuous glucose monitor values.
9. You may take additional fingerstick readings as desired.
10. You will use the continuous glucose monitor with the hypoglycemia alarm set at 70 mg/dL and the hyperglycemia alarm set at 260 mg/dL during the days prior to testing. On the last two days of the Control Week, the CGM hypoglycemic alarm will be set at 90 mg/dL. If either of the continuous glucose monitor alarms, a fingerstick value will be obtained.
11. You will be instructed to follow the Home Glycemic Safety Protocol (handout).
12. In addition to device-required calibrations, an additional calibration will be performed prior to the evening meal +/- 30 minutes to minimize the likelihood that a calibration is requested close to the time of the study meal. The continuous glucose monitor will be calibrated per manufacturer's guidelines with the study glucometer.
13. You will have access to ad lib glucose-free beverages.
14. You will continue with the data collection process as described during Days 2-6.
15. Study personnel will be in frequent contact with you during this phase of the study.
16. You will be asked to confirm the time and content of meals and snacks when they occur. They will also notify study personnel of fingerstick values.
17. You will be asked to be at home with comparable physical activity level as the Experimental Admission.
18. Data will be downloaded from all devices at the end of the Experimental and Control Admissions.

PROCEDURES RELATED TO THE SUBSTUDY (DAYS 18-22):

The substudy may occur at any time during the primary study protocol. The study team will request 5-8 people to participate in this portion of the study. Your willingness to participate in the substudy is independent of your participation in the main study.

1. You will wear the Accu-Chek Spirit Combo pump during the entire substudy (5 days). Specific training will be given for the Accu-Chek Spirit Combo including the Accu-Chek Aviva Combo device. This training will occur as a separate outpatient visit or while admitted to the Center for Diabetes Technology Research House during the primary study based on your convenience. A study pump used for training purposes will be utilized. A qualified staff member will conduct the training and in particular discuss differences from their home pump in important aspects such as calculation of insulin on board.
2. The Accu-Chek Spirit pump will be programmed with your usual basal rates from 07:00 to 10:00 PM. DiAs will be turned on in open loop between 8:00 - 10:00 PM. The study pump will be programmed for

a basal rate from 10:00 PM – 07:00 AM. This will allow for DiAs to operate. If there is any unforeseen delay of more than 15min in initiating DiAs in open loop, a basal rate will be entered into the Accu-Chek Spirit Pump until connection can be established.

3. After 07:00 AM, you may leave the research study house and participate in their usual activities (work, home) during the day. **Activities should be similar to the 5 day period #1 of continuous glucose monitor -augmented insulin pump therapy during the main study.** For example, if you worked during the 5 day data collection period, we will ask that you maintain your work schedule as close as possible. If you exercised at a certain time, we will ask that you maintain your exercise schedule. You and the study physician may discuss specific activities to see if they will impact the study. You will be asked to remain within the greater Charlottesville area during this time period. You will have unlimited access to study MD and qualified medical study personnel by phone, email, text or in person if needed to address any concerns during the day with use of the pump or other clinical concerns.
4. You will be asked to return to the research study house by 6:00 PM.
5. The study pump and continuous glucose monitor will be downloaded.
6. Dinner will occur between 6:00 – 7:00 PM.
7. Hypoglycemic treatments can occur at any time per your request. In addition, you will follow the Home Glycemic Safety Protocol (handout).
8. You will start the DiAs in open loop mode between 8:00 - 10:00 PM. When DiAs is operating, the Accu-Chek Aviva Combo Device will be removed from the vicinity of the DiAs.
9. You may administer correction boluses at any time prior to 11:00 PM per your usual regimen.
10. The system will turn on Safety System and the Basal Rate Modules at 11:00 PM to 07:00 AM similar to the experimental session.
11. At approximately 11:00 PM, lights will be turned out, and you will be encouraged to sleep.
12. The staff will be checking the readings of the secondary continuous glucose monitor receiver at 03:00 AM and 05:00 AM during the night and will monitor you remotely. Additional readings may be taken as necessary.
13. Continuous glucose monitors will be calibrated in the same manner as described in Procedures Related to the Experimental Procedures.
14. You will be awakened shortly before 7:00 AM and allowed time for routine hygiene.
15. A fingerstick value will be obtained upon waking while you are still fasting.
16. At 7:00 AM, DiAs will be stopped and you will resume continuous glucose monitor-augmented insulin pump therapy. These same procedures will be repeated for 5 consecutive nights. You will be able to leave the Research House each morning if blood glucose is 80-249 mg/dl and the glucose trend is stable. A meal will be offered to you.

STUDY SCHEDULE

Study Procedures	Screening	Study Training	Data Collection	Sensor Insertion	Experimental Admission	Control Admission	Phone Check In	Substudy
Visit	**1**	**2**	**X**	**X**	**3**	**4**	**5**	**6**
Days	**1**	**2**	**2-7 & 10-15**	**24-48 hours before Exp Adm**	**7-9 or 15-17**	**7-9 or 15-17**	**18-19 or 23-24**	**18-22**
Duration	**2 hours**	**~2 hours**	**5 days**	**15 min**	**~40 hours**	**~40 hours**	**5-15 min**	**5 days**
Location	**OPTX**	**OPTX**	**OPTX**	**OPTX**	**Guest House**	**OPTX**	**OPTX**	**Guest House**
Informed Consent	X							
Clinical exam & medical history	X							
Inclusion/Exclusion Criteria	X							
Screening Labs	X							
Urine pregnancy test women who are able to become pregnant		X			X			
Discuss medication and meal boluses	X	X			X		X	
CGM Insertion		X		X				
DiAs					X			X
Current Medication Review	X	X			X			
Discuss medication and meal boluses	X	X			X		X	
Identical meals, snacks & exercise					X	X		
Fingersticks similar to each admission					X	X		
Equipment Downloads			X ** (Day 6&14)		X	X		
Wearing Study Insulin Pump					X			X
Use Safety Protocols					X	X		X

OPTX = Outpatient

~means approximately

** You will be asked to download your insulin pump data on Day 2 or 3 to ensure accurate record keeping.

Blood Testing

We will take up to 2 tablespoons of blood for the study (taken during the screening visit). The blood we take will be tested to measure your diabetes control, your thyroid function, how well your kidneys/liver work, the amount of certain salts and sugars, and to see if you are pregnant (females). When these tests are done, any remaining sample will be thrown away. It will not be stored for any future testing.

You will be asked to check perform fingersticks at least 4 times daily.

If you want to know about the results before the study is done:

During the study you are having an investigational test done. The purpose of the test is NOT to diagnose any disease or abnormality you may have. Because the test is investigational there is no way for the study leader to understand if the results are "normal" or "abnormal". However, if any test results are concerning, your study leader will let you know. The study physician may also discuss these findings with your PCP or Endocrinologist.

In addition, as the research moves forward, your study leader will keep you informed of any new findings about the research itself that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

Risks related to treating type 1 diabetes with an insulin pump (with or without using a Control to Range system):

Likely

- Risk of possible mild to moderate low blood sugar and possible symptoms of low blood sugar, such as sweating, trembling, difficulty thinking, dizziness, and feeling uncoordinated.
- Risk of possible mild to moderate high blood sugars and possible symptoms of high blood sugars such as thirst and frequent urination

Rare but serious

- Risk of severe temporary low blood sugar (hypoglycemia) that can lead to unconsciousness, hypoglycemic seizure, hospitalization or even death.
- Risk of prolonged high blood sugar leading to diabetic ketoacidosis, hospitalization, and even death.

Risks associated with continuous glucose monitor insertion:

Likely:

- Failure or lack of sensitivity of the continuous glucose monitor sensor that requires replacement / insertion of new sensor
- Fingerstick for calibration of the continuous glucose monitor

- Discomfort from insertion of sensor

Less Likely:

- Bruising less than ½ inch
- Bleeding less than ¼ teaspoon
- Sensitivity to adhesives with use of continuous glucose monitor resulting in skin irritation, redness, blistering, scarring, systemic allergic reaction or secondary skin infection

Rarely:

- Swelling or redness at insertion site
- Psychological reaction to viewing the continuous glucose monitor information or attending to continuous glucose monitor alarms or fingerstick blood glucose values.
- Breakage of the continuous glucose monitor sensor under the skin with possible symptoms of skin irritation and inflammation. If a sensor breaks and no portion of it is visible above the skin, do not attempt to remove it. Please call the study team or seek immediate medical assistance. Seek professional medical help if you have symptoms of infection or inflammation – redness, swelling or pain – at the insertion site.

Risk of symptoms related to the insulin pump site insertion:

Rarely:

- Sensitivities to adhesives associated with insulin catheter resulting in skin irritation, swelling, redness, blistering, scarring, nodular reactions, systemic allergic reaction or secondary skin infection
- Bruising greater than ¼ inch
- Bleeding greater than 1/8 teaspoon of blood

Risks and side effects related to blood glucose collection via fingerstick:

Likely:

- Pain at site of lancet (finger-pricking needle) use
- Bleeding at site of lancet use

Less Likely:

- Incorrect information from a false low or false high fingerstick or HemoCue reading

Rarely:

- Infection at site of lancet use

Risks associated with performing a serum (blood) or urine pregnancy tests (women who are able to become pregnant):

Less Likely:

- False positive or false negative results

Risks associated with staying at the research house:
Likely

- Loss of privacy and disruption of daily routine similar to staying at a bed and breakfast

Risk of sharing the Continuous Glucose Monitor
We will use the continuous glucose monitor equipment with other study subjects. The sensors will not be shared. The transmitter wirelessly sends your glucose information from the sensor to the receiver. The transmitter, which snaps into the sensor, will be cleaned thoroughly with a diluted mixture of bleach or another appropriate cleaner after use. The FDA approved the continuous glucose monitor as a 'single use device'. This means that they recommend that only one person use this device as there is a rare risk that a bloodborne pathogen, such as Hepatitis B, may be spread if used with multiple patients.

Risk of sharing the Insulin Pump (Experimental Admission only):
We will use the hand-held Accu-Chek Spirit Insulin Pump with other study subjects. All infusion set equipment (infusion set insertion kits, tubing, cartridges, and the Aviva Combo glucometer) will not be shared. The Accu-Chek Spirit Insulin Pump handheld device will be reused after cleaning thoroughly with a diluted mixture of bleach or another appropriate cleaner after use. The FDA approved the Accu-Chek Combo System (insulin pump & Aviva glucometer) for 'single-patient use'. This means that they recommend that only one person use this device as there is a rare risk that a bloodborne pathogen, such as Hepatitis B, may be spread if used with multiple patients.

Risks of having your blood drawn:
Having blood drawn may cause:

- ✓ pain (common),
- ✓ a bruise (sometimes),
- ✓ fainting or passing out (not very often),
- ✓ infection (rare), and
- ✓ vein swelling, vein inflammation, or a blood clot in the vein (rare).

If the people doing the study are exposed to your blood or body fluids in a way that could give them a disease, your blood may be tested. The tests might check for:

- ✓ hepatitis,
- ✓ HIV (Human Immunodeficiency Virus), or
- ✓ other infections.

You and the person exposed would be told the test results. However, your name would be kept private. If your test is positive for hepatitis or HIV, we will tell you how to find counseling. You may want help in understanding what the results mean for you.

Other unexpected risks:
You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Risks of Videotaping/Audio taping:
With your permission, we may photograph or videotape your participation in this trial. Photographs and videotapes will be used in presentations at conferences, potential study subjects, and potential research donors. Your willingness to have photos taken is independent of your participation in this trial. Your photo or videotape will not used without your consent. Your identity can remain anonymous.

☐ I agree to be photographed/videotaped during this trial.

_____
Initials

☐ I agree to be photographed/videotaped during this trial but would like to remain anonymous.

_____
Initials

☐ I do **NOT CONSENT** to being photographed/videotaped during this trial.

_____
Initials

Risks for women:
You must use an approved form of birth control during this study. You will be told to ask your doctor for more details about the proper birth control method. If you become pregnant during this study, you are told to inform your study doctor right away. Your study doctor will discuss her treatment and the effect of the study on your pregnancy.

Other unexpected risks:
You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?
You will not benefit from being in this study. However the information researchers get from this study may help others in the future.

What are your other choices if you do not join this study?
You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include continuing your home insulin regimen.

If you are a patient at UVa, your usual care will not be affected if you decide not to participate in this study. If you are an employee of UVa, your job will not be affected if you decide not to participate in this study.
If you are an employee of UVa your job will not be affected if you decide not to participate in this study. If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will be paid $335 for finishing the 17 day study. If you choose to participate in the substudy, you will be compensated an additional $100 at its completion. These payments will be a check from the University of Virginia**.** You should get your payment about six weeks after finishing the study. The income may be reported to the Internal Revenue Service (IRS) as income.

If you do not finish the study, you will be paid as follows:

- Study Training (Visit 2): $30
- Experimental Admission (Visit 3): $135
- Control Week Completion (Visit 5): $135
- Compensation for Test Strips: $35
- Substudy Completion: $100

If the study leader says you cannot continue, you will be paid for the visits that you have completed.

You will not be paid at all if **you** decide not to finish this study. If you are sick and cannot participate in the study admission, then you will not get paid until your study admission is rescheduled and completed. If the study leader decides to stop your study, you will be paid the full amount for the study.

If you owe money to any Virginia state agency, the state can use the money you earn in this study to pay those debts. These state agencies include the UVa Medical Center, Virginia Commonwealth University (VCU) Medical Center or a college or university. The money may be withheld to pay back debt for such things as unpaid medical bills, taxes, fines, child support. Even if this happens, the money you earn may be reported to the Internal Revenue Service (IRS) as taxable income.

Reimbursement for meal receipts (if necessary):*:*
Since you have to have the exact meals on during Control Admission and your Experimental Admission, grant money will be used to pay for these meals. Study staff may purchase your meals. If you purchase your own meals during the Control Admission, we will ask that you provide a receipt to the study team within 30 days for a refund.

You should get your reimbursement about 30 days after you submit your meal receipts to the study team.

If you owe money to any Virginia state agency, the state can use the money you earn in this study to pay those debts. These state agencies include the UVa Medical Center, VCU Medical Center or a college or university. The money may be withheld to pay back debt for such things as unpaid medical bills, taxes, fines, child support.

Will being in this study cost you any money?

Being in this study will not cost you any money. Your insurance company will also not be billed.

- The insulin pump and the continuous glucose monitor will be provided to you to use in during the trial.
- At the end of the study, you will be permitted to keep the study glucometer, but all other equipment will be returned to the study team.
- You will use your own insulin.

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask for an estimate of your financial costs. You may also wish to check with your insurance company before the study starts. Ask what they will cover and if they require you to get their permission before you decide to be in the study.

You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

If you are hurt as a result of being in this study, there are no plans to pay you for lost wages, disability, or discomfort. The sponsor will reimburse the reasonable cost of necessary and appropriate emergency and/or acute medical care for injury or illness that is determined by the principal investigator and sponsor to be directly related to the study. Injury related to the study does not include the normal progression of any disease or any underlying pre-existing medical conditions. If you have questions about what will be covered if you are hurt in the study, talk to the principal investigator. You do not give up any legal rights, such as seeking compensation for injury, by signing this form.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health

b) Your disease gets worse
c) The side effects of the treatment are too dangerous for you
d) New information shows the treatment will not work or is not safe for you
e) You do not follow your doctor's instructions
f) The study sponsor closes the study for safety, administrative or other reasons

If you decide to stop being in the study and you are wearing the study insulin pump or continuous glucose monitor, we will ask you to return it to the Center for Diabetes Technology. The insulin pump and continuous glucose monitors remain property of the study sponsor and will need to be returned. If you decide to stop being in the study and are not wearing the study insulin pump or continuous glucose monitors, we ask that you notify the research team so any admissions scheduled may be cancelled.

How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address, date of birth,
- Social Security number ONLY IF you are being paid to be in this study
- Your health information. If required for this study, this may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers (if required for this study, this may include mental health care records, substance abuse records, and/or HIV/AIDS records).

Who will see your private information?

- The researchers to make sure they observe the effects of the study and understand its results
- People or committees that oversee the study to make sure it is conducted correctly
- People who pay for the study (NIH)
- Insurance companies
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors that make the device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA)
- Researchers from outside of UVa may be present during your study visits. They will be observing to learn how to conduct this study and to train on the use of the equipment in order to conduct the trial at their own sites in the future.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

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.

The University of Virginia has granted the Center for Diabetes Technology the use of a facility designated home to perform the outpatient studies related to the Artificial Pancreas Project. The guesthouse is a 4 bedrooms/4 bath home. The study team may test 3-4 study participants at the same time. Consequently, there are important confidentiality issues that you may want to consider when participating in this trial:

- A bedroom will be designated specifically for your use, but you may need to share a bathroom with another study participant.
- Study staff will introduce you to other study participants by using only your first name. Any other level of personal information (i.e. last name, profession, etc.) disclosed to other participants is your choice.
- Both men and women may be admitted to the guesthouse at the same time.
- Other participants may witness the study team attending to your needs (i.e. when your blood glucose level is low or high). Other participants do not have access to the DiAs information on your cell phone.
- Internet service is available for your use, but the IP addresses of any personal devices (laptop, tablet, smartphone, etc.) used to access the internet via the house's network will be tracked and visible to those people and entities that have access to the network traffic and physical system.

ZIP Folder:
Data from your equipment may be downloaded and submitted to the study team. We strongly recommend submitting your data in an encrypted folder attached to an otherwise blank email. The study team will provide you instructions on how to do this. We are requesting an encrypted folder and a blank email to add additional security to your private information within these files. Should you decide to attach the unencrypted, separate files in an email to the study team, you are accepting the risk that your information may be compromised. Email messages, by themselves, are not secure and even if your home or work computer is on a protected server, the email may pass through an unsecure server in transit.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation. UVa researchers will do everything possible to protect your privacy.

However, they will need to share your information with people who may not have to follow the rules described above. Some of those people may be allowed to share/release your information without your permission.

A copy of this consent form will be put in your medical record. (This is not the same as the record of this research study.) This means that everyone who is allowed to see your records will be able to find out that you are in this study.

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Sue Brown, M.D.
University of Virginia
Department of Endocrinology & Metabolism
Box 400888 Charlottesville, VA 22908
Phone: 434-924-0000 pic: 2046

What if you have a concern about a study?

You may also report a concern about a study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483
Charlottesville, Virginia 22908 Telephone: 434-924-2620

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Would you like to be considered to participate in the substudy at the conclusion of the primary study?

_____ ☐ I would like to be considered to participate in the substudy.
Initials

_____ ☐ I do **NOT** want to be considered for the substudy.
Initials

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this document after you have signed it.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE