UVA CENTER FOR DIABETES TECHNOLOGY

Evaluation of The Postprandial Impact of Automated Priming Bolus for Full Closed Loop Insulin Delivery

Protocol Chair

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Center for Diabetes Technology

NCT#05528770

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KEY ROLES

Protocol Principal Investigator	
Name, degree	Sue Brown, MD
Institution Name	University of Virginia Center for Diabetes Technology

PROTOCOL VERSION HISTORY

Version Number	Author(s)	Approver	Effective Date	Revision Description
1.0	Mark DeBoer, Mary Oliveri	Sue Brown	29-Jul-2022	Original Protocol
1.1	Mary Oliveri	Mark DeBoer	15-Aug-2022	FDA requested mods: • Figure 1 was updated • BPS transitions described (section 7.6)
1.2	Mark DeBoer	Mark DeBoer	16-Aug-2022	FDA requested mods: • Inclusion & exclusion criteria (section 3.5 & 3.6) • Pilot study BPS corrections (section 6.3 & 6.4) • Exercise termination criteria (section 7.8) • Discharge criteria (section 7.9) • Individual stopping criteria (section 11.10.1)
1.3	Mary Oliveri	Sue Brown	23-Aug-2022	FDA requested mods: • Pilot study will complete a minimum of 2-3 participants (section 1.3, 3.2 & Chapter 6) • A H&P within 9 months of screening appointments may be used (section 3.4 & 3.7) • Further modified Exercise termination criteria (section 7.8) • Discharge criteria (section 6.6)
1.4	Mary Oliveri	Sue Brown	12-Sep-2022	IRB Pre-Review mods (07-Sep-2022): • Clarified enrollment numbers (section 3.2 & 13.2) • Edited inclusion criteria (section 3.5). • Edited Screening Process (section 3.4 & 3.7) • Deleted references to questionnaires (section 5.1, 7.2, & 7.10) • Added 5-minute low intensity warm up (section 7.7) • Clarified Covid testing (section 9.1.3) • Deleted Covid vaccination record (section 10.3)

				• Edited pre-screening description (section 3.7)
1.5	Sue Brown	Sue Brown	25-Sep-2022	IRB FB Review request: • SAP description (Chapter 13).
1.6	Mary Oliveri	Mary Oliveri	27-Sep-2022	IRB FB Review request: • Remove screening remote references
1.7	Mary Oliveri	Mary Oliveri	06-Oct-2022	IRB FB Review request: • Clarified Part 11 identification process (section 15.3.1)

SITE PRINCIPAL INVESTIGATOR STATEMENT OF COMPLIANCE

Protocol Title: Evaluation of The Postprandial Impact of Automated Priming Bolus for Full Closed Loop Insulin Delivery

Protocol Version/Date: v1.7 06-Oct-2022

I have read the protocol specified above. In my formal capacity as a Site Principal Investigator, my duties include ensuring the safety of the study participants enrolled under my supervision. It is understood that all information pertaining to the study will be held strictly confidential and that this confidentiality requirement applies to all study staff at this site.

This trial will be carried out in accordance with ICH E6 Good Clinical Practice (GCP) and as required by the following: United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

As the Principal Investigator, I will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), or other approved Ethics Committee, except where necessary to eliminate an immediate hazard(s) to the trial participants.

All key personnel (all individuals responsible for the design and conduct of this trial) have completed Human Participants Protection Training and Good Clinical Practice Training. Further, I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitments.

Investigator's Signature _____Date: _____ / _____ / _____

Investigator's Name: _____

Site Name: University of Virginia

LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
ADRR	Average Daily Risk Range
AP	Artificial Pancreas
BG	Blood Glucose
BT/BTLE	Bluetooth, Bluetooth low energy
BPS	Bolus Priming System
CGM	Continuous Glucose Monitoring
CLC	Closed-Loop Control
CSII	Continuous Subcutaneous Insulin Injection
DKA	Diabetic Ketoacidosis
DSMB	Data Safety Monitoring Board
FCL	Fully Closed Loop
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HbA1c	Hemoglobin A1c
HBGI	High Blood Glucose Index
HIIT	High-intensity interval training
HCL	Hybrid Closed Loop
IDE	Investigational Device Exemption
IOB	Insulin-on-Board
LBGI	Low Blood Glucose Index
POC	Point-of-Care
QC	Quality Control
UI	User Interface

PROTOCOL SUMMARY

PARTICIPANT AREA	DESCRIPTION
Title	Evaluation of The Postprandial Impact of Automated Priming Bolus for Full Closed Loop Insulin Delivery
Investigational Device	UVA Model Predictive Control Artificial Pancreas (RocketAP) with and without use of the Bolus Priming System (BPS)
Objectives	The purpose of this study is to show the safety and feasibility of a new fully automated AP controller with and without the Bolus Priming System
Study Design	A randomized cross-over trial assessing glycemic responses to a fully automated AP system using two approaches: 1) using the Bolus Priming System (which detects shifts in glucose level to trigger a priming dose of insulin) 2) without the Bolus Priming System We will also have structured meal and exercise challenges of the fully closed loop system.
Number of Sites	One
Endpoint	The primary outcome will be time in range 70-180 mg/dL for a 24-hour period.
Population	Key Inclusion Criteria • Age 18 and ≤65 years of age • Clinical diagnosis, based on investigator assessment, of type 1 diabetes for at least one year • Currently using insulin for at least six months • Currently using insulin pump for at least three months
Sample Size	• **Pilot Study:** complete a minimum of 2-3 participants • **Main Study**: complete up to 20 participants
Treatment Groups	Randomized crossover: Participants will be randomized to the order that they experience the use of the BPS in fully automated closed loop (FCL) (for 24 hours each, with a 24-hour washout in between): 1) with the BPS active, 2) without BPS.
Participant Duration	**Pilot Study:** Participants will be admitted to a local hotel or rental house for up to approximately 24 hours and will have a dinner with the RocketAP without the BPS **Main Study:** Participants will be admitted to a local hotel for approximately 96 hours.
Protocol Overview/Synopsis	Main Study participants will be admitted to the hotel for a 4-night study, receiving the two sessions in random order: 1) FCL with BPS activated, 2) FCL without the BPS, with a 24-hour washout period in between. During the admission, participants will receive structured meals and have blood glucose control followed to compare time in range 70-180 mg/dL between Controller sessions. After the first 24 hour period on the first FCL approach (BPS vs. no BPS,) that the participant has been randomized to, there will be a 24 hour challenge period before shifting to the other randomized approach; during this session participants will undergo further testing of the control algorithm, including meal challenges and a high-intensity interval training bout.

STUDY VISITS AND PROCEDURES SCHEDULE

	Screening	Study Equipment Training	Pre-Admission Check-In	Study Admission	Post-Admission Check-In
Location	**Clinic**	**Clinic/ Remote**	**Phone/ Email/ Text**	**Hotel/Rental House**	**Phone/ Email/ Text**
Visit	**1**	**2**	**3**	**4**	**5**
Informed Consent	**X**				
Eligibility Assessment	**X**				
Medical History	**X**				
HbA1c	**X**				
Pregnancy test (if applicable)	**X**	**X**		**X**	
Physical Exam	**X**				
Vital Signs (height/weight)	**X**			**X**	
Electrocardiogram (ECG)	**X**				
Demographic Survey	**X**				
Randomization				**X**	
COVID-19 Testing			**X**		
CGM Use				**X**	
Survey	**X**				
Review diabetes management and AEs				**X**	**X**

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Chapter 1 Background

1.1 Introduction

A major impediment to maintaining blood glucose (BG) control in Type 1 diabetes (T1D) is missed meal boluses, which has been associated with significantly higher HbA1c levels.[1] While the advent of the artificial pancreas (AP) offers promise of safe reductions in HbA1c, our research group previously found that current AP systems only partly compensates for missed prandial insulin.[2] We thus designed a new system called RocketAP to be fully automated, utilizing a Bolus Priming System (BPS) that recognizes meal ingestion and delivers a quick priming dose of insulin prior to extreme blood sugar excursions. When used as a fully automated closed loop (FCL) system (without any meal announcements to the controller), this system improves time-in-range compared to a current commercially available system (Control-IQ). However, we have not previously determined whether the BPS provides improved blood sugar control over what the RocketAP controller could without the BPS. Indeed, when the BPS provides a bolus, it reduces the amount of insulin the controller can provide in response to high blood sugars—leaving open the possibility that the RocketAP controller could provide a similar degree of blood sugar control after unannounced meals. In addition, this system needs to be further tested under challenging conditions of exercise and food intake. This is particularly true for the BPS, given the potential that the BPS could detect spurious changes in blood sugar and provide a priming dose of insulin in the absence of a meal.

In the current study, the maximum amount of insulin that the BPS injects (which varies based on the system's calculation of the probability that a meal has been ingested) is 6% of the person's total daily insulin for any individual meal. This system is equipped with a novel hypoglycemia anti-rebound system, which constrains insulin infusion after CGM/SMBG readings<70 mg/dL. The BPS system is also silenced at night (23:00 – 6:00h).

In the current study, we are testing this RocketAP system for BG levels using two approaches:

A randomized cross-over trial where each participant will experience FCL for two 24-hour study periods in random order (referred to as FCL1 and FCL2) with:

- The BPS functioning
- The BPS inactivated

During the washout period between FCL1 and FCL2, we will test the RocketAP system in FCL with further challenges, both before and after the change in BPS treatment arm—i.e., not as a cross-over assessment but a comparison between participants randomized to start with or without BPS. These challenges will include:

- A session of high-intensity interval training (assessing the safety of the BPS when BG's may spike during bursts of anaerobic activity)

- A high-carbohydrate, high-fat meal (assessing how the system responds to prolonged carbohydrate absorption)
- Ingestion of a bolus of simple sugar (assessing the safety of the BPS when the user's blood sugar spikes from a relatively low amount of carbohydrate)

Participants will be admitted to a hotel and started on the RocketAP for the purpose of comparing FCL use with and without BPS as described above, all implemented on the DiAs platform (MAF 2109). As an assessment of the efficacy of the system in maintaining BG control, participants will be followed for approximately 24 hours in the randomized phase (FCL1 vs. FCL2) and during the 24-hour cross-over phase. Our primary outcome will be one of efficacy in assessing BG control (TIR 70-180 mg/dL) between the two 24-hour FCL1/FCL2 periods.

We hypothesize that performances of RocketAP without BPS in FCL will provide similar glycemic control as FCL with BPS. We expect that this will constitute an important step toward having a fully automated AP system because it may remove the need for a BPS system that itself could increase risk of episodes of hypoglycemia.

1.2 Study Objective

The purpose of this study is to test the performance of the RocketAP in FCL both with and without the BPS, assessing efficacy and safety. We will target completion of up to 20 adults in a randomized cross-over trial, comparing blood glucose time in range 70-180 mg/dL for two 24-hour periods and assessing TIR during an additional challenge period, which will be compared between those who started on BPS vs. those who did not.

1.3 Study Design

We will consent up to 30 participants, ages ≥18.0 and ≤65 years, with a goal to have up to 20 participants complete the trial. The study will be performed overnight at a local hotel/rental house (heretofore referred to as "hotel"). Enrollment in the Pilot Study will proceed with the goal of completing a minimum of 2-3 participants. This admission will be about 24 hours at a hotel/rented house. Enrollment in the Main Study will proceed with the goal of completing 20 participants.

1.3.1 Study Hardware/Software

The study itself will involve use of the DiAs prototyping platform (MAF 2109), connected to a Tandem t:AP research pump and a Dexcom G6 sensor, and implementing RocketAP with and without BPS. Upon arrival at the hotel, participants will be instructed in how to use the Tandem research pump as well as the UVa AP system, including stopping the system.

1.3.2 Timing of UVa Artificial Pancreas Use

The participants will arrive to hotel the evening before starting the experimental system to allow for a settling of blood glucose in an unfamiliar environment. The next morning, participants will be connected to a Tandem research pump connected to the UVa DiAs platform and their Dexcom

G6 Transmitter will be linked with DiAs. Participants will then be taught how to use DiAs in this configuration. The research pump will be programmed with the individual's usual insulin parameters. Once started, the participants will have their blood sugar managed through this system during the entirety of the time at hotel.

1.3.3 Study Controller Sessions

Order and timing of controller sessions: During the hotel stay, participants will have two separate 24-hour periods during which they will receive FCL control with and without the BPS active. These will be separated by a 24-hour challenge period which will involve further challenges. The timing and potential order of these sessions is shown in Figure 1.

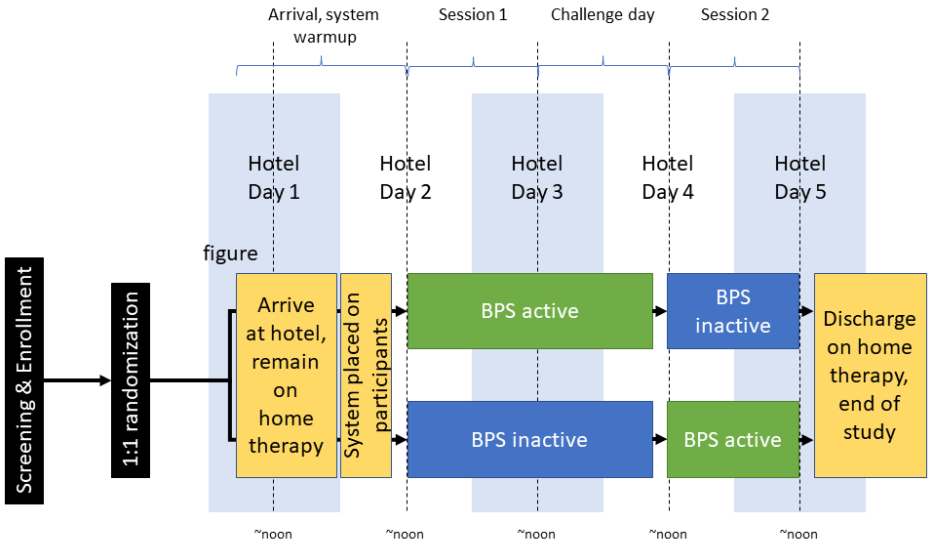

Figure 1: Timeline and randomized order of the Study Controller Sessions

During these 24-hour periods participants will be followed for the experimental meals as part of the Study Controller Sessions to compare blood glucose control with and without the BPS (Figure 1). The study meals and activities will be standardized between study sessions (see Figure 2).

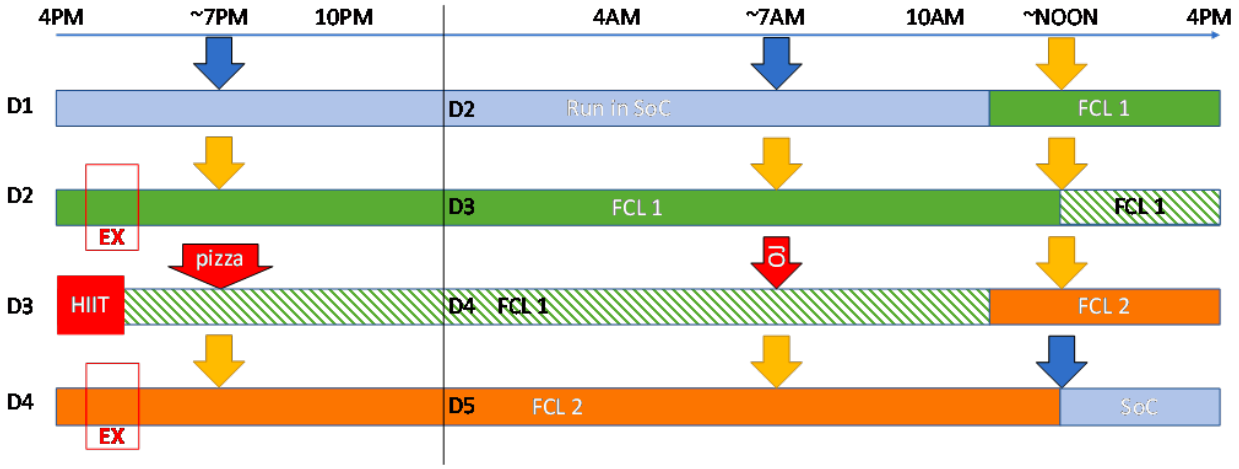

Figure 2: Timeline of Study Controller Sessions and Study Meals and activities. There will be two identical 24-hour periods (FCL1 in green and FCL2 in orange), separated by a 24-hour challenge period (FCL1 in green-hatched) that will first involve the BPS activation assignment the participant was randomized to (the treatment approach used in FCL1) and then involve the alternate assignment (the treatment approach to be used in FCL2), with the system switch at the end of the challenge day. Arrows represent meals with Blue Arrows representing meals in which the participants are using their personal devices.

The primary outcome will compare the percent time CGM is between 70 and 180 mg/dL during daytime for FCL1 and FCL2 sessions with and without BPS. During the time between arrival at the hotel and being started on the experimental system, participants will use their home diabetes management approach, including insulin dosing via normal carbohydrate announcement. Starting the first morning of the study (Day 2 of study), study staff who will be present will include nursing staff and technical staff; a study physician will be available either on-site or nearby off-site at all times. Hyperglycemia and hypoglycemia treatment protocols will be followed per guidelines. We anticipate more significant cases of hyperglycemia during meals on the study system because of the lack of carbohydrate announcement; participants will be encouraged to drink large amounts of non-caloric beverages, particularly after these meals. UVa CDT study staff will monitor CGM output continuously and manage glucose control issues. At the end of the hotel stay, the participant will return to their home insulin management.

1.4 Study Device Download

Before discharge from the hotel, all study devices will be turned in to study staff for device download, and the participants will return to their usual diabetes management.

1.5 Study System Issues

If the CGM signal becomes unavailable for more than 20 minutes consecutively, closed loop will not operate to automatically adjust insulin. If the CGM is not connected, the system will revert to usual function of the pump and deliver insulin with the insulin dosing parameters programmed in

the system for that individual. Resumption of closed-loop control will occur automatically once CGM signal is available again.

If the study system is unable to maintain pump connectivity, the pump will automatically revert to pre-programmed basal insulin delivery after 30 minutes without any need for instruction from the user.

Chapter 2 Study Devices

2.1 Insulin Pump

The study systems will utilize the Tandem t:AP research pump connected to the UVa DiAs system run on a dedicated external smart phone, running the RocketAP control algorithm with either the BPS system active or not, with the order of these sessions determined randomly.

2.2 Continuous Glucose Monitor

The study CGM will include Dexcom G6 transmitter and sensors. The CGM sensor is viable for 10 days.

2.3 Blood Glucose Meter and Strips

Blood glucose levels will be measured during the hotel admission with the use of a study glucometer. The CGM device will be calibrated, if needed, using the study glucometer and strips in accordance with the manufacturer's labelling.

2.4 Ketone Meter and Strips

Blood ketone levels will be measured during the hotel admission with the use of the Abbott Precision Xtra meters and strips in accordance with the manufacturer's labelling. The blood glucose meter component of the Precision Xtra Device will not be used.

2.5 Study Devices Accountability Procedures

Device serial numbers will be recorded, and use of equipment will be tracked.

Chapter 3 Study Screening

3.1 Clinical Sites

The study will be performed at the University of Virginia, with screening procedures taking place either virtually, at the Clinical Research Unit, or at local hotel.

3.2 Participant Recruitment and Enrollment

Pilot Study: Enrollment goal in the Pilot Study will be to complete a minimum of 2-3 participants. Up to 6 participants may sign consent forms.

Main Study: Enrollment in the study will proceed with the goal of completing up to 20 participants. Participants will initially be randomized for the order of using FCL with or without BPS. Up to 30 participants may sign the consent form.

3.3 Informed Consent and Authorization Procedures

Before consent has been obtained, participants will be asked inclusion/exclusion criteria questions during pre-screening to determine study eligibility. Before completing any procedures or collecting any data that are not part of usual care, written informed consent, when applicable) will be obtained. Potential eligibility may be assessed as part of a routine-care examination.

A participant is considered enrolled when the informed consent form has been signed by the participant and the study team.

Consenting procedures and documentation is defined in section 15.3.

3.4 Screening Procedures

After informed consent has been signed, a potential participant will be evaluated for study eligibility through the elicitation of a medical history, performance of a physical examination by licensed personnel, an ECG, and pregnancy testing (if applicable) to screen for exclusionary medical conditions.

A physical exam documented in the prior 9 months can suffice for the physical exam but will not serve as an exclusionary criterion if not available. Participants may self-report height, weight, blood pressure, temperature, and heart rate . Individuals who do not initially meet study eligibility requirements may be rescreened at a later date per investigator discretion.

3.5 Participant Inclusion Criteria

The participants must meet all of the following inclusion criteria in order to be eligible to participate in the study.

1. Age ≥18.0 and ≤65 years old at time of consent
2. Clinical diagnosis, based on investigator assessment, of type 1 diabetes for at least one year

3. Currently using insulin for at least six months
4. Currently using insulin pump for at least three months
5. Using insulin parameters such as carbohydrate ratio and correction factors consistently on their pump in order to dose insulin for meals or corrections
6. Current regular exercise (e.g. walk, bike, jog) and be able to participate in a high intensity interval training activity.
7. Access to internet and willingness to upload data during the study as needed
8. For females, not currently known to be pregnant or breastfeeding
9. If female and sexually active, must agree to use a form of contraception to prevent pregnancy while a participant in the study. A negative serum or urine pregnancy test will be required for all females of childbearing potential. Participants who become pregnant will be discontinued from the study. Also, participants who during the study develop and express the intention to become pregnant within the timespan of the study will be discontinued.
10. Willingness to suspend use of any personal CGM for the duration of the clinical trial once the study CGM is in use
11. Willingness to use the UVa closed-loop system throughout study admission
12. Willingness to use personal lispro (Humalog) or aspart (Novolog) during the study admission.
13. Willingness not to start any new non-insulin glucose-lowering agent during the course of the trial (including metformin/biguanides, GLP-1 receptor agonists, pramlintide, DPP-4 inhibitors, sulfonylureas and naturaceuticals)
14. Willingness to eat at least 1 g/kg of carbohydrate per day during the hotel admission
15. Willingness to reschedule if placed on oral steroids
16. An understanding and willingness to follow the protocol and signed informed consent
17. Willingness to follow COVID-19 protocols in place at the time of study.

3.6 Participant Exclusion Criteria

The participant must not have any exclusion criteria in order to be eligible to participate in the study.

1. History of diabetic ketoacidosis (DKA) in the 6 months prior to enrollment
2. Severe hypoglycemia resulting in seizure or loss of consciousness in the 12 months prior to enrollment
3. Pregnancy or intent to become pregnant during the trial
4. Currently being treated for a seizure disorder
5. Planned surgery during study duration.
6. Treatment with meglitinides/sulfonylureas at the time of hotel study.

7. Use of metformin/biguanides, GLP-1 agonists, pramlintide, DPP-4 inhibitors, SGLT-2 inhibitors, or naturaceuticals with a change in dose in the past month.
8. Coronary artery disease or heart failure, unless written clearance is received from a cardiologist or personal health care provider allowing clearance for high-intensity interval training and documentation of a negative stress test within the year
9. History of cardiac arrhythmia (except for benign premature atrial contractions and benign premature ventricular contractions which are permitted or previous ablation of arrhythmia without recurrence which may be permitted)
10. Clinically significant electrocardiogram (ECG) at time of Screening, as interpreted by the study medical physician.
11. A known medical condition that in the judgment of the investigator might interfere with the completion of the protocol such as the following examples:
    a. Inpatient psychiatric treatment in the past 6 months
    b. Presence of a known adrenal disorder
    c. Abnormal liver function test results (Transaminase >2 times the upper limit of normal); testing required for subjects taking medications known to affect liver function or with diseases known to affect liver function
    d. Uncontrolled thyroid disease
    e. Musculoskeletal or other condition that limits participation in exercise portion of study
12. A known medical condition that in the judgment of the investigator might interfere with the completion of the protocol.
13. Positive Covid-19 test result

3.7 Visit 1: Screening Procedures

The participant will be evaluated for study inclusion and exclusion eligibility after the informed consent form has been signed by the participant and the study team.

Individuals who do not initially meet study eligibility requirements may be rescreened at a later date per investigator discretion.

Screening procedures will last approximately 1-2 hours. The visit may occur in-person or by telecommunication. The following procedures may be performed/data collected/eligibility criteria checked and documented:

1. Inclusion and Exclusion criteria assessed
2. Demographics, including:
    a. Date of birth
    b. Gender
    c. Race
    d. Ethnicity
3. Medical History, including diabetes history

   a. Duration of disease (number of years)
   b. Current insulin pump model
   c. History of CGM use
   d. Current treatment
   e. Severe hypoglycemia history
   f. Severe hyperglycemia history
   g. History of seizures
   h. Loss of consciousness
4. Basal rates
5. Carbohydrate ratios
6. Insulin sensitivity factors
7. Target glucose
8. Average daily insulin
9. Surgical history
10. Allergies
11. Concomitant medications
12. Electrocardiogram (ECG)
13. Physical Examination – Aa historical history and physical report within 9 months of screening appointments may be used but is not required for eligibility. If vitals are not available, may include self-reported values.
   a. Weight (may be self-reported)
   b. Height (may be self-reported)
   c. Blood pressure
   d. Temperature
   e. Heart Rate
14. Screening Labs
   a. Hemoglobin A1c point of care
   b. Urine or serum pregnancy test for all women of childbearing potential (this test can be done remotely with results sent to the study team)

If needed based on medical history, investigators may include baseline chemistry panel, liver function tests, hematocrit, and thyroid stimulating hormone (lab results within one year of screening appointment may be used).

Up to 6 months of historical data from the participant's personal insulin pump, glucometer, or continuous glucose monitor may be downloaded or recorded. Data will be obtained from the participant's personal insulin pump and CGM. This data may be obtained through the commercial applications (e.g. t:connect and Dexcom G6).

If participants are on-site, the participant's glucometer may be uploaded to ensure that the participant can successfully upload the equipment.

Any labs required may be obtained at a local laboratory (e.g. LabCorp) convenient to the participant.

This study is not meant to find out if the participant has any other disease or problem. The study leaders will alert the participant if any of the research results are important to his/her health during the study. The participant may have a copy of the screening tests to discuss with the personal physician. When the blood tests are completed, any blood left over will be thrown away. It will not be stored for any future testing.

For potential subjects who live out of state and or a significant distance from UVA to facilitate the consent process, e-consent will be used. Note: For potential participants who are not able to use DocuSign, email, fax, or mail will be an option for receipt of the signed consent. The consenting process will involve discussing the study at length in a phone call/HIPAA compliant telecommunication method with the interested potential participant. The potential participant will be asked permission to review inclusion/exclusion criteria to assess if they are eligible to participate in the study. If permission is granted, the study team will review the pre-screening questionnaire which contains the inclusion/exclusion criteria. If eligible, the study team member will provide a copy of the informed consent form (i.e. in person, email, or mail) to the potential participant for their review. Potential participants may also elect to choose to review the informed consent form prior to discussing pre-screening questions.

The potential participant will be given an opportunity to ask the study team questions or may speak directly with the study physician. After ample time to make an informed decision, the potential participant may sign the consent form at home and provide it to the study team (e.g. in person, electronically, email, fax, or mail). The potential participant's understanding of the information, presented in the process of consent will be assessed by asking open-ended questions, may occur during the phone call or at the screening appointment. Once consent is obtained, study procedures may begin (e.g. LabCorp).

The study physician or physician designee will have the discretion to repeat screening tests. The repeat screening tests may be conducted locally (e.g. LabCorp). The participant may request a copy of any of the results from the screening evaluation to review with their primary care provider.

If an exclusionary condition is identified, the study participant will be excluded from participation with follow up and referral to their primary care physician as needed.

If the study participant is pregnant, the study physician will discuss the results of the blood test with the participant and the participant will be asked to seek confirmation of the test and the appropriate medical care.

Participants may be re-screened at a later date if their clinical situation changes as determined by the study physician.

3.8 Demographic Data Survey

Research in diabetes technology has revealed significant disparities in minoritized population's representation in clinical trials and access to devices that improve diabetes outcomes. Collection

of detailed demographic data regarding participants in technology trials has become essential. This includes data on race/ethnicity, income levels and insurance status, as well as education and other variables that describe the study population.

The Demographic Data Survey will be electronically administered once eligibility has been met.

a. Gender
b. Race
c. Ethnicity
d. Marital status
e. Level of education
f. Employment status
g. Household income
h. Health insurance status
i. Monthly insulin costs

Chapter 4 Randomization

Participants will receive the two different experimental conditions (FCL with and without BPS) in random order as described below.

4.1 Pilot Study Participants

Pilot participants will not be randomized and will use the RocketAP system with and without BPS.

4.2 Main Study Participants

Once eligibility is met and screening procedures are completed, the participant may continue to randomization. Screening failures and study dropout participants may be replaced. Randomization will occur via permuted blocks of 4.

Chapter 5 Visit 2: Study Equipment Training

Equipment training may begin at the hotel after UVa AP system has been put in place. The purpose of this training is to introduce the study insulin pump and study CGM to the participant.

The participant's insulin parameters will be programmed into their study insulin pump and confirmed by two research staff. Subjects will then switch to the study insulin pump. The participant's personal pump and infusion site will be removed.

The participant will have the insulin pump and sensor on them at all times.

5.1 CGM Training

A study CGM will be provided to all participants at the training session. The participants will be provided with CGM equipment and instructed to use the study CGM on a daily basis. If the participant has prior use of the CGM, re-training will be specific to the individual. The study team may elect to have less frequent CGM users watch the Dexcom online training videos (https://www.dexcom.com/training-videos) to assist in the training session. Study staff training may include review of study CGM in real-time to make management decisions and how to review the data after an upload for retrospective review. Study staff will specifically identify how alarms are set using the app and the frequency that these alarms will repeat.

The participants personal CGM will be discontinued. The participants will be observed placing the sensor and will learn/review how to access the CGM trace via the DiAs phone or the Tandem research pump, as needed. The participants will be asked to perform fingerstick blood glucose measurements (if needed) in accordance with the labelling of the study CGM device.

An electronic copy of the CGM user's guide will be provided for the participants to read. The study team will be sure that the participants will leave the training session knowing how to properly use the CGM. The study team will be available for any questions.

Participants will have the option of using their personal smartphone or receive a study smartphone to use in order to collect the data from the devices. If the participant elects to use a personal device, the Dexcom app will be downloaded to their phone in order to monitor the participant's CGM values and alerts in real-time may be used.

5.2 Activity Tracker

All participants may be asked to wear an activity tracker (e.g. Fitbit) during the entire study (home and hotel admissions) to record information about movement and heart rate though not an endpoint in this study.

5.3 Study Insulin Pump

The study team will be responsible for monitoring and managing the study insulin pump during the hotel admissions. The participants may be provided a quick overview on its functionality to understand the equipment.

5.3.1 Study Insulin Pump Topics

The study team will assist the participant in study pump infusion site initiation and will start the participant on the study pump. The study pump will be programmed with the participant's usual basal rates and pump parameters. The participant's personal pump will be removed. The investigator may elect to use an existing personal pump infusion site at their discretion at the start of the study.

The participant will be instructed on charging the pump, navigation through menus, bolus procedures including stopping a bolus, etc.

5.3.2 Other Issues

The participant will be instructed to notify study staff if they experience any issues with the study devices during the hotel admission. Staff will be present in the event that if insulin is delivered by any means other than the study pump (e.g. injection of subcutaneous insulin via syringe in the event of infusion site failure). If insulin is delivered by any means other than the study pump, the study team will be instructed to turn off closed-loop mode for approximately four hours.

The participant will also be asked to alert the study clinical staff for technical issues with the Tandem research pump and/or the DiAs system, including use of the study pump and study CGM (open loop mode) during periods of component disconnections or technical difficulties.

A glucagon emergency kit will be available at the hotel once the investigational system is in place.

Glycemic Treatment Guidelines will be available for staff use during the study admissions.

5.3.3 Optimization of Insulin Pump Settings

Data-driven optimization of pump settings can occur any time prior to the hotel admission, particularly if the participant contacts the study physician due to concerns about their pump settings due to recurring hypo- or hyperglycemia. No pump settings changes can occur during closed loop testing.

Chapter 6 Pilot Study

In order to optimize the flow of the study visits during the Main Study, we will perform a Pilot Study at a local hotel or rental house. The duration of the pilot admission will be approximately 24 hours with the intent of testing the logistics of our study procedures. The goal will be to complete 2-3 participants. Pilot study participants are eligible to enroll in the Main Study.

Participants and staff will adhere to the Covid-19 Mitigation Plan as outlined in Section 10.3

6.1 Qualifications and Role of the Staff

For the pilot study, there will be at least two study staff present at all times at the study site, at least one of whom will be clinical staff (e.g. nurse, physician, nurse practitioner, physician assistant). There will be a physician available either on-site or off-site within an approximate 20-minute drive at all times. In addition, one of the study medical physicians and one senior engineer will be on call during the entire admission. Glucagon for the emergency treatment of hypoglycemia will be available on-site.

6.2 Visit 3: Pre-Admission Check-In Visit

Pilot participants will be contacted by the study team approximately 24-48 hours prior to the hotel admission to verify the following information:

- Inquire about any changes to the participant's medical history
- Study equipment (e.g. CGM and activity tracker) initiation has occurred
- Determine pump profile(s) the participant uses on certain days
- New CGM sensor has been placed approximately 24-72 hours prior to admission for proper warm-up
- Verify with the participant that the goal CGM reading on day 2 is less than 200 mg/dL; this may require contact with the study physician prior today 2 of the hotel study.
- Should any concerns regarding medical history, pump information, or unforeseen issues arise, the admission will be cancelled for that participant at the discretion of the investigator

6.3 Visit 4: Admission Check-In

For the pilot study, one to three participants will be assessed at a time. The participant will arrive at the hotel on the first day of the admission. The study team will perform vital signs and inquire about any changes to the participant's medical history. Any changes to medical history will be communicated to the medical physician to ensure continued eligibility and participation.

A urine pregnancy test will be collected if relevant. The test must be negative for the participant to continue with the study.

The subject's CGM reading, and ketone concentration will be recorded. In the event that the participant's CGM reading is not between 80-250 mg/dL or ketone concentration is ≥0.6 mmol/L prior to initiation of the UVa AP system, the study physician may recommend additional insulin

dosing according to the participants' usual doses. Study physician may elect to cancel participant's participation in the hotel admission if concerned about their medical safety. This participant will not be replaced.

The participant's home insulin pump will be discontinued, and the study Tandem research insulin pump will be initiated using the RocketAP system with BPS activated. The study team will ensure the proper function of the CGM, insulin pump, and activity tracker. The goal will be to initiate Closed-Loop Control by approximately lunch time, running the RocketAP system on the DiAs platform.

The CGM used in the study is FDA-approved for the non-adjunctive measurement of blood glucose (i.e. the CGM reading can be used for insulin dosing decisions). The CGM readings will be the primary source of blood glucose values. There are no protocol fingerstick blood glucose measurements other than at times of CGM calibration (if necessary) and if directed by the study team. Fingerstick blood glucose measurements may be taken whenever participants experience symptoms, if the CGM glucose is suspected to be erroneous, or any time the participant would like to be reassured.

6.4 Study Meals

Participants will eat a structured dinner at approximately 6-7 pm during the admission. The participant will not announce carbohydrate ingestion, allowing testing of the RocketAP controller with BPS following dinner. Breakfast in the morning will be with the BPS system engaged. Throughout the Pilot study, the participant will remain in closed loop mode.

6.5 Admission Activities

In the afternoon after admission, participants will participate in a supervised bout of high-intensity interval training (see details in Section 7.8). During this time, the system will have BPS activated. Apart from the programmed exercise portions, participants will be free to engage in low-intensity activity (i.e. walking) during the admission. Participants will enjoy quiet activities in the evening.

6.6 Admission Discharge

Discharge will be at approximately noon. Discharge criteria is CGM value 80-300 mg/dL with stable trend and ketones <=0.6 mmol/L. If the CGM values are above 300 mg/dL and ketone values are >0.6 mmol/L, the study team will check the insulin pump infusion site and correction insulin will be administered per study physician judgement via the subject's insulin pump. A qualified clinical study team member (e.g. MD, NP, PA, CDE) will assess and discuss the transition back to usual care with the study participant.

Participants will be asked to continue monitoring ketone levels for 24-48 hours after the hotel admission if ketones were >0.6 mmol/L at time of discharge. Urine ketone supplies may be provided for this testing.

6.7 Visit 5: Post Admission Check-In Visit

Approximately 24-48 hours after the hotel admission, the study team will contact the participant via phone/email/text/text to assess adverse events, adverse device effects, and device issues.

Chapter 7 Main Study

7.1 Hotel Admission

Main Study participants will participate in hotel admission. Each admission will be up to approximately 96 hours in duration.

Participants and staff will adhere to the Covid-19 Mitigation Plan as outlined in Section 10.3.

7.2 Qualifications and Role of the Staff

There will be at least two study staff present at all times at the study site, at least one of whom will be clinical staff (e.g. nurse, physician, nurse practitioner, physician assistant). There will be a physician at the hotel or nearby on call during the study at all times. In addition, at least one senior engineer will be on call during the entire admission. Participants will be remotely monitored by at least one study team member using a web-based remote monitoring system that has been previously established for DiAs. The web-based remote monitoring system will display real-time insulin delivery, CGM and other system information to allow for patient safety monitoring. In addition, study team members will be trained in all protocol and glycemic treatment guideline procedures. The closed-loop system will be managed by the participant with study-staff supervision, particularly at the time of insulin boluses. Glucagon for the emergency treatment of hypoglycemia will be available on-site.

7.3 Visit 3: Pre-Admission Check-In Visit

Participants will be contacted by the study team approximately 24-48 hours prior to each hotel admission if most recent contact with the study participant exceeds 10 days. The study team will verify the following information:

- Inquire about any changes to the participant's medical history
- Study equipment (e.g. CGM and activity tracker) initiation has occurred
- Determine pump profile(s) the participant uses on certain days
- New CGM sensor has been placed approximately 24-72 hours prior to admission for proper warm-up
- Verify with the subject that the goal CGM reading at time of arrival is less than 200 mg/dL; this may require contact with the study physician prior to arrival on the day of the study visit
- Should any concerns regarding medical history, pump information, or unforeseen issues arise, the admission will be cancelled for that participant at the discretion of the investigator

7.4 Visit 4: Admission Check-In

Participants will arrive at the hotel on the first day of the admission. As described in section 10.3, all participants will receive a test for COVID-19 after arriving for the study. The study team will perform vital signs and inquire about any changes to the participant's medical history. Any

changes to medical history will be communicated to the medical physician to ensure continued eligibility and participation.

A urine pregnancy test will be collected for female participants of childbearing age. The test must be negative for the participant to continue with the study.

The subject's CGM reading, and ketone concentration will be recorded. In the event that the participant's CGM reading is not between 80-250 mg/dL or ketone concentration is ≥0.6 mmol/L prior to initiation of the UVa artificial pancreas system, the study physician may recommend additional insulin dosing according to the participants' usual doses. Study physician may elect to cancel participant's participation in the hotel admission if concerned about their medical safety. This participant will not be replaced.

The participant's home insulin pump will be discontinued, and the study insulin pump will be initiated. The study team will ensure the proper function of the CGM, insulin pump, and activity tracker.

The CGM used in the study is FDA-approved for the non-adjunctive measurement of blood glucose (i.e. the CGM reading can be used for insulin dosing decisions). The CGM readings will be the primary source of blood glucose values. There are no protocol fingerstick blood glucose measurements other than at times of CGM calibration (if necessary) and if directed by the study team. Fingerstick blood glucose measurements may be taken whenever participants experience symptoms, if the CGM glucose is suspected to be erroneous, or any time the participant would like to be reassured. Glycemic Treatment Guidelines to be used during the hotel admission are defined in a separate document.

7.5 System Transitions

Participants will be informed beforehand and at the time of the transfer from one BPS state to another. Participants will be told what this transition means with respect to insulin dosing. The transfer from one treatment to another will proceed as follows:

- The system is stopped
- DiAs is plugged into a laptop and 'parameters.xml' file (with the corresponding BPS condition) will be replaced
- DiAs is restarted
- CGM is recovered and pump connections is checked
- DiAs is transitioned to Closed Loop Control mode

7.6 Study Meals

Participants will eat structured study meals during the admission, with the same amount of carbohydrate, protein and fat for meals (breakfast, lunch, dinner) on the days for FCL1 and FCL2). During the 24-hour challenge period, there will be additional meal challenges that will only be performed on that day. This includes a high carbohydrate high fat meal at dinner (such as pizza)

and an early breakfast that consists primarily of fast-acting carbs (e.g.. juice). In all cases the carbohydrate content of the meal will not be announced during the study once the AP system has been placed. Snacks with carbohydrates will not be allowed unless for the treatment of low blood sugars. Non-carbohydrates snacks may be allowed throughout the protocol per investigator discretion, but the intention is not to have non-carbohydrate snacks. Blood glucose levels will be followed via continuous glucose monitor and glucose values will be managed by the AP system as usual.

7.7 Admission Activities

During the study, we will challenge the participants with exercise sessions that will be supervised by study staff. During FCL1 and FCL2, participants will do a mild to moderate walking or similar exercise at approximately 4pm on each of those study days.

During the challenge phase (the 24-hour period between the FCL1 and FCL2), participants will undergo supervised session of high-intensity interval training (HIIT). The HIIT workout will consist of a 5-minute low intensity warmup period, a workout of about 1 minute of vigorous exercise followed by approximately 2 minutes of light intensity exercise or rest. This 3-minute set of intervals may be repeated up to 6 times or until volitional exhaustion, followed by approximately 5 minutes of light intensity cooldown and stretching. The goal of this will be to assess the safety of the AP system in HIIT, given that HIIT has been observed to result in an increase in BG levels, which could theoretically lead to activation of the BPS—dosing insulin. The AP system will be monitored for BPS activation during this workout. If the BPS is activated, participants will continue to be monitored for BG excursions, including receiving treatment for hypoglycemia if this occurs (as described in the Glycemic Treatment Guidelines).

Exercise challenges will be terminated early with subjective symptoms such as shortness of breath, chest pain, dizziness, palpitations, or any such concerning symptoms reported by participants. Participants will stop their participation in the exercise portion of the study if reporting any concerning symptoms. Study physicians (or physician's assistants) will assess the participants for their need for additional care outside the study. If symptoms resolve entirely and there is no additional requirement for care outside the study, participants will stop participation in the exercise portion of the study and will not repeat that portion of the study. Participants however may then continue with the remainder of the study per investigator discretion.

Participants will also be free to engage in low-intensity activity (i.e. walking) during the hotel admission but will be asked to have this match between 24-hour study periods as best as possible. Participants may leave the hotel to be outside, provided they are accompanied by a study staff member and follow COVID precautions in place at the time of study, as described in Section .3. Participants will enjoy quiet activities in the evening.

7.8 Admission Discharge

Discharge will be at approximately 1 pm. Discharge criteria is CGM value 80-300 mg/dL with stable trend and ketones <=0.6 mmol/L. If the CGM values are above 300 mg/dL and ketone values are >0.6 mmol/L, the study team will check the insulin pump infusion site and correction insulin will be administered per study physician judgement via the subject's insulin pump. A qualified clinical study team member (e.g. MD, NP, PA, CDE) will assess and discuss the transition back to usual care with the study participant.

Participants will be asked to continue monitoring ketone levels for 24-48 hours after the hotel admission if ketones were >0.6 mmol/L prior to discharge. Urine ketone supplies may be provided for this testing.

All study equipment will be returned at the time of study end. Per investigator discretion, a participant may wear home the study CGM device in use and will be requested to return the study transmitter.

7.9 Visit 5: Post Admission Check-In Visit

Approximately 24-48 hours after the hotel admission, the study team will contact the participant via phone/email/text to assess adverse events, adverse device effects, and device issues.

7.10 Medical Monitor Review

At the conclusion of the Main Study, the medical monitor will review the data as referenced in section 8.3.

Chapter 8 Medical Monitor Review

8.1 Medical Monitor Study Safety Data Review

The Medical Monitor will be provided all adverse event data for review to assess safety. The Medical Monitor will review data related to individual stopping criteria as detailed in the study protocol.

8.2 Medical Monitor Main Study Safety Data Review

A Medical Monitor will review compiled safety data at the conclusion of the trial. In addition, the Medical Monitor will review all DKA and severe hypoglycemia irrespective of relatedness to study device use, and all serious events (including UADEs) related to study device use at the time of occurrence. The Medical Monitor also will be informed of any ADEs not meeting criteria for a UADE if the Study PI requests the Medical Monitor review. The Medical Monitor can request modifications to the study protocol or suspension or stoppage of the study if deemed necessary based on the totality of safety data available.

Chapter 9 Testing Procedures

9.1 Laboratory / Point of Care Testing

9.1.1 HbA1c

A blood sample will be obtained at screening to obtain a baseline hemoglobin A1c level. A blood test obtained within 2 weeks prior to enrollment may be used.

HbA1c level may be measured by study team using the DCA2000, a comparable point of care device, at time of screening

Labs may be obtained at a local laboratory (e.g. LabCorp) convenient to the participant.

9.1.2 Pregnancy Test

A serum or urine pregnancy test will be required for women of childbearing potential at in person visit and admission. Test must be negative to participate in the study.

9.1.3 Covid-19 Testing

All participants and study staff (e.g. on-site research coordinators, technicians, nurses, and physicians) will be tested with a COVID-19 test within the first 24 hours of the hotel admission or up to 72 hours in advance of being on-site for the Pilot and Main Study. Individuals with Covid-19 positive tests will be excluded from the study.

9.1.4 Demographic Data Survey

The Demographic Data Survey will be asked after study eligibility has been met.

Chapter 10 Risks Associated with Clinical Trial

10.1 Potential Risks and Benefits of the Investigational Device

Risks and Benefits are detailed below. Loss of confidentiality is a potential risk; however, data are handled to minimize this risk. Hypoglycemia, hyperglycemia and ketone formation are always a risk in participants with type 1 diabetes and participants will be monitored for these symptoms.

10.1.1 Venipuncture Risks

A hollow needle/plastic tube may be placed in the arm for taking blood samples (e.g. external HbA1c measurements for inclusion criteria). Blood draws can cause some common reactions like pain, bruising, or redness at the sampling site. Less common reactions include bleeding from the sampling site, formation of a small blood clot or swelling of the vein and surrounding tissues, and fainting.

10.1.2 Fingerstick Risks

About 1 drop of blood will be removed by fingerstick for measuring blood sugars and sometimes HbA1c or other tests. This is a standard method used to obtain blood for routine hospital laboratory tests. Pain is common at the time of lancing. In about 1 in 10 cases, a small amount of bleeding under the skin will produce a bruise. A small scar may persist for several weeks. The risk of local infection is less than 1 in 1000. This should not be a significant contributor to risks in this study as finger sticks are part of the usual care for people with diabetes.

10.1.3 Subcutaneous Catheter Risks (CGM)

Participants using the CGM will be at low risk for developing a local skin infection at the site of the sensor needle placement. If a catheter is left under the skin for more than 24 hours it is possible to get an infection where it goes into the skin, with swelling, redness and pain. There may be bleeding where the catheter is put in and bleeding under the skin causes a bruise (1 in 10 risk).

Study staff should verbally alert the participant that on rare occasions, the CGM may break and leave a small portion of the sensor under the skin that may cause redness, swelling, or pain at the insertion site. The participant should be further instructed to notify the study coordinator immediately if this occurs.

10.1.4 Risks of Hypoglycemia

As with any person having type 1 diabetes and using insulin, there is always a risk of having a low blood sugar (hypoglycemia). The frequency of hypoglycemia should be no more and possibly less than it would be as part of daily living. Symptoms of hypoglycemia can include sweating, jitteriness, and not feeling well. Just as at home, there is the possibility of fainting or seizures (convulsions) and that for a few days the participant may not be as aware of symptoms of

hypoglycemia. A CGM functioning poorly and significantly over-reading glucose values could lead to inappropriate insulin delivery.

10.1.5 Risks of Hyperglycemia

Hyperglycemia is likely because of the study design including unannounced carbohydrate ingestion. Also, hyperglycemia and ketonemia could occur if insulin delivery is attenuated or suspended for an extended period or if the pump or infusion set is not working properly. A CGM functioning poorly and significantly under-reading glucose values could lead to inappropriate suspension of insulin delivery.

10.1.6 Risks of Device Reuse

Participant will be informed that FDA or relevant national authorities have approved the insulin pump, CGM, glucometer and ketone meter for single use and that by using them among multiple patients, bloodborne pathogens (i.e. Hepatitis B) may be spread through the use of multiple users.

The study CGM system is labelled for single use only. The sensor (the component of the system that enters the skin) will be single use only. The transmitter and receiver may be reused during the study after cleaning the device using a hospital-approved cleaning procedure. The transmitter is attached to the sensor but does not enter the skin and the receiver, if used, is a handheld device.

The study insulin pumps are labelled for single-patient use. During the study, this device may be reused after cleaning adhering to a hospital-approved cleaning procedure. All infusion set equipment will be single patient use only (infusion set insertion kits, tubing, cartridges etc.).

The study blood glucose meter and blood ketone meter are labelled for single-patient use. During the study, these devices may be reused after cleaning adhering to a hospital-approved cleaning procedure.

10.1.7 Device Cleaning Instructions

CGM cleaning instructions are provided in the Dexcom G4 Platinum (Professional) Cleaning and Disinfection manual (current edition) and a similar approach will be applied for the G6 version used in this study. The transmitter should be cleaned with Clorox Healthcare® Bleach Germicidal Cleaner or any disinfectant product in a spray bottle containing a bleach solution of 6500 parts per million with the EPA registration number 56392-7. The transmitter will be submerged in this solution and then placed on an absorbent wipe or clean surface. Two sprays will be dispensed from the Clorox cleaner onto each side of the transmitter. A nylon brush will be used to scrub the transmitter on all sides for 30 seconds. The transmitter will be placed in the Clorox Cleaner solution for one minute. Transmitter is then rinsed under flowing tap water for ten seconds. The transmitter will then be disinfected using a disinfectant product with EPA registration number 56392-7 using similar procedures as the cleaning process.

Per the pump manufacturer, the insulin pump will be cleaned with a damp lint-free cloth. Use of household or industrial cleaners, solvents, bleach, scouring pads, chemicals, or sharp instruments are prohibited. The pump should never be submerged in water. If needed, use only a very mild detergent, such as a bit of liquid soap with warm water. A soft towel will be used to dry the pump.

The glucometer is cleaned and disinfected with two separate Super Sani-Cloths (EPA number 9480-4). The entire surface will be cleaned, making sure the surface stays wet for 2 minutes. This step is repeated with a clean cloth for disinfecting the device.

The Precision Xtra User's Guide suggests that healthcare professionals use 10% bleach, 70% alcohol or 10% ammonia to clean the device.

Equipment that touches intact skin will be cleaned with ethyl or isopropyl alcohol (70-90%), quaternary ammonium germicidal detergent (i.e. Cavicide, EPA number 46781) or household bleach. The contact time on the surface depends on the method used to clean the equipment. Cavicide requires three minutes on the surface of the equipment. Clorox Germicidal Bleach Wipes require two minutes on the equipment. The surface should remain wet (i.e. slightly damp) with the disinfectant to be considered effective though not wet enough to leave drops of liquid.

In the event a manufacturer updates cleaning procedures for their device, the study team will adhere to the most current recommendations.

There is the risk of blood sampling collection and contamination from sampling techniques. Hand washing with either soap & water or waterless hand sanitizer will be used prior to caring for the study subject. Gloves will be worn during blood sample collection and processing. Medical personnel will continue to practice hygiene for the subject's protection (i.e. hand washing, changing gloves frequently, disposing needles properly). Gloves will be removed, and hands washed or sanitized prior to leaving and upon return to the subject's room. Soiled linen will be changed to minimize the transfer of pathogenic organisms.

10.1.8 Risk of Exercise

There is a risk of musculoskeletal symptoms or injury from participating in an exercise regimen. There are cardiovascular or cerebrovascular risks (including but not limited to dizziness, lightheaded, syncope, arrhythmia or ischemia) associated with participating in an exercise regimen. The intention of the eligibility criteria will be to minimize these risks.

10.1.9 Hb1Ac Risk

An NGSP Point of Care analyzer (i.e. DCA Vantage Analyzer) will be utilized at the research site to obtain the subject's HbA1c level.

10.1.10 Other Risks

Some participants may develop skin irritation or allergic reactions to the adhesives used to secure the CGM, or to secure the insulin infusion sets for the continuous subcutaneous insulin infusion. If these reactions occur, different adhesives or "under-taping" (such as with IV 3000, Tegaderm, etc.) will be tried, sites will be rotated frequently, and a mild topical steroid cream or other medication may be required.

Whenever the skin is broken there is the possibility of an infection. The CGM and pump infusion sites are inserted under the skin. It is possible that any part that is inserted under the skin may cause an infection. These occur very infrequently, but, if an infection was to occur, oral and/or topical antibiotics can be used. The risk of skin problems could be greater if you use a sensor for longer than it is supposed to be used. Therefore, participants will be carefully instructed about proper use of the sensor.

Data downloaded from the CGM, pump, glucometer, and ketone meter will be collected for the study as measures of diabetes self-management behaviours. Some people may be uncomfortable with the researchers' having such detailed information about their daily diabetes habits.

10.1.11 Known Potential Benefits

It is expected that this protocol will yield increased knowledge about using an automated closed-loop system with anticipatory action to control glucose levels. The individual participant may not benefit from study participation.

10.1.12 Risk Assessment

Based on the facts that (1) adults with diabetes experience mild hypoglycemia and hyperglycemia frequently as a consequence of the disease and its management, (2) the study intervention involves periodic automated insulin dosing that may increase the likelihood of hypoglycemia, and periodic automated attenuation of insulin delivery that may increase the likelihood of hyperglycemia, (3) mitigations are in place, and have been tested in prior studies using the investigational device system in the home setting, that limit the likelihood of excessive insulin dosing or prolonged withdrawal of insulin, and (4) rapid reversal of hypoglycemia and hyperglycemia can be achieved.. In addition, it is the belief of the investigators that this study also presents prospect of direct benefit to the participants and general benefit to others with diabetes.

10.2 General Considerations

The study is being conducted in compliance with the policies described in the study policies document, with the ethical principles that have their origin in the Declaration of Helsinki, with the protocol described herein, and with the standards of Good Clinical Practice (GCP).

Whenever possible, data will be directly collected in electronic case report forms, which will be considered the source data.

The protocol is considered a significant risk device study, due to the fact that the closed-loop system is experimental. Therefore, an investigational device exemption (IDE) from the U.S. Food and Drug Administration (FDA) is required to conduct the study.

10.3 COVID-19 Risk Mitigation Plan and Justification

The study team will follow local guidelines that are in effect at the time of the study admission.

10.3.1 Participants and Study Personnel

We will follow a combination of approaches to increase our likelihood of having a COVID-free environment:

- We will follow CDC and local guidelines in effect at the time of the study.
- All participants and study staff (research coordinators, technicians, nurses, and physicians) will be tested with an FDA authorized COVID-19 test with the **first 24 hours of study start or up to approximately 72 hours before their participation in the study hotel**. Those with positive tests will be excluded from the study.
- Any participants with positive test will be discharged from the study. Hotel rooms of these participants will be restricted from future use. We will limit any personal interaction between study personnel and these individuals. We will follow local guidelines in effect at the time of study to guide interactions.

10.3.2 Environment

The study team will adhere to current hotel guidelines.

Chapter 11 Adverse Events, Device Issues, and Stopping Rules

11.1 Definitions

11.1.1 Adverse Events (AE)

Any untoward medical occurrence in a study participant, irrespective of the relationship between the adverse event and the device(s) under investigation (section 11.2) for reportable adverse events for this protocol).

Positive pregnancy test will be not considered adverse event.

11.1.2 Serious Adverse Event (SAE)

Any untoward medical occurrence that:

- Results in death.
- Is life-threatening; (a non-life-threatening event which, had it been more severe, might have become life-threatening, is not necessarily considered a serious adverse event).
- Requires inpatient hospitalization or prolongation of existing hospitalization.
- Results in persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions (life threatening).
- Is a congenital anomaly or birth defect.
- Is considered a significant medical event by the investigator based on medical judgment (e.g., may jeopardize the participant or may require medical/surgical intervention to prevent one of the outcomes listed above).

11.1.3 Unanticipated Adverse Device Effect (UADE)

Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants (21 CFR 812.3(s)).

11.1.4 Adverse Device Effect (ADE)

Any untoward medical occurrence in a study participant which the device may have caused or to which the device may have contributed.

11.1.5 Device Complaints and Malfunctions

A device complication or complaint is something that happens to a device or related to device performance, whereas an adverse event happens to a participant. A device complaint may occur independently from an AE, or along with an AE. An AE may occur without a device complaint or there may be an AE related to a device complaint. A device malfunction is any failure of a device

to meet its performance specifications or otherwise perform as intended. Performance specifications include all claims made in the labelling for the device. The intended performance of a device refers to the intended use for which the device is labelled or marketed. (21 CFR 803.3).

11.2 Reportable Events

For this protocol, a reportable adverse event includes any untoward medical occurrence that meets one of the following criteria:

- A serious adverse event as defined in section 11.2
- An Adverse Device Effect as defined in section 11.1.4, unless excluded from reporting in section 11.7
- An Adverse Event as defined in section 11.1.1 occurring in association with a study procedure
- An AE as defined in section 11.1.1 which leads to discontinuation of a study device for 2 or more hours
- Hypoglycemia meeting the definition of severe hypoglycemia as defined in section 11.2.1
- Diabetic ketoacidosis (DKA) as defined in section 11.2.2 or in the absence of DKA, a hyperglycemic or ketosis event meeting the criteria defined below

Hypoglycemia and hyperglycemia not meeting the criteria below will not be recorded as adverse events unless associated with an Adverse Device Effect. Skin reactions from sensor placement are only reportable if severe and/or required treatment.

11.2.1 Hypoglycemia Event

Hypoglycemia not associated with an Adverse Device Effect is only reportable as an adverse event when the following definition for severe hypoglycemia is met:

- The event required assistance of another person due to altered consciousness, and required another person to actively administer carbohydrate, glucagon, or other resuscitative actions
- Impaired cognitively to the point that he/she was unable to treat himself/herself, was unable to verbalize his/ her needs, was incoherent, disoriented, and/or combative, or experienced seizure or coma. These episodes may be associated with sufficient neuroglycopenia to induce seizure or coma
- If plasma glucose measurements are not available during such an event, neurological recovery attributable to the restoration of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration

11.2.2 Hyperglycemia Events/Diabetes Ketoacidosis

Hyperglycemia not associated with an Adverse Device Effect is only reportable as an adverse event when one of the following four criteria is met:

- The event involved DKA, as defined by the Diabetes Control and Complications Trial (DCCT) and described below evaluation or treatment was obtained at a health care provider facility for an acute event involving hyperglycemia or ketosis

- Blood ketone level ≥1.5 mmol/L and communication occurred with a health care provider at the time of the event
- Blood ketone level ≥3.0 mmol/L, even if there was no communication with a health care provider

Hyperglycemic events are classified as DKA if the following are present:

- Symptoms such as polyuria, polydipsia, nausea, or vomiting
- Serum ketones ≥1.5 mmol/L or large/moderate urine ketones
- Either arterial blood pH <7.30 or venous pH <7.24 or serum bicarbonate <15
- Treatment provided in a health care facility

All reportable Adverse Events—whether volunteered by the participant, discovered by study personnel during questioning, or detected through physical examination, laboratory test, or other means—will be reported on an adverse event form online. Each adverse event form is reviewed by the Medical Monitor to verify the coding and the reporting that is required.

11.3 Relationship of Adverse Event to Study Device

The study investigator will assess the relationship of any adverse event to be related or unrelated by determining if there is a reasonable possibility that the adverse event may have been caused by the study device.

To ensure consistency of adverse event causality assessments, investigators should apply the following general guideline when determining whether an adverse event is related:

- There is a plausible temporal relationship between the onset of the adverse event and the study intervention, and the adverse event cannot be readily explained by the participant's clinical state, intercurrent illness, or concomitant therapies; and/or the adverse event follows a known pattern of response to the study intervention; and/or the adverse event abates or resolves upon discontinuation of the study intervention or dose reduction and, if applicable, reappears upon rechallenge.
- Evidence exists that the adverse event has an etiology other than the study intervention (e.g., pre-existing medical condition, underlying disease, intercurrent illness, or concomitant medication); and/or the adverse event has no plausible temporal relationship to study intervention.

11.4 COVID-19 Transmission

While we are taking steps to prevent transmission of COVID-19 during this study, there is a possibility that participants, based either on exposure before the hotel admission or during the stay, are infected with COVID-19. Any appearance of significant COVID-19 symptoms in participants will be cause for repeat COVID-19 testing and possible quarantine until test results are returned. If this Covid-19 test is positive, the participant will be discharged from the study.

In the event of a COVID-19 positive test in a participant, the study team will follow up with the participant via phone until conclusion of treatment for the COVID-19 related symptoms. All

participants will be asked to follow up via phone with the study team in the event of a positive test within 14 days after discharge from the hotel.

11.5 Intensity of Adverse Event

The intensity of an adverse event will be rated on a three-point scale: (1) mild, (2) moderate, or (3) severe. It is emphasized that the term severe is a measure of intensity: thus, a severe adverse event is not necessarily serious. For example, itching for several days may be rated as severe, but may not be clinically serious.

- MILD: Usually transient, requires no special treatment, and does not interfere with the participant's daily activities.
- MODERATE: Usually causes a low level of inconvenience or concern to the participant and may interfere with daily activities but is usually ameliorated by simple therapeutic measures.
- SEVERE: Interrupts a participant's usual daily activities and generally requires systemic drug therapy or other treatment.

11.6 Coding of Adverse Events

Adverse events will be coded per the UVA IRB website instructions (i.e. mild, moderate, severe). The Medical Monitor will review the investigator's assessment of causality and may agree or disagree. Both the investigators and Medical Monitor's assessments will be recorded. The Medical Monitor will have the final say in determining the causality.

Adverse events that continue after the participant's discontinuation or completion of the study will be followed until their medical outcome is determined or until no further change in the condition is expected.

11.7 Outcome of Adverse Events

The outcome of each reportable adverse event will be classified by the investigator as follows:

- RECOVERED/RESOLVED – The participant recovered from the AE/SAE without sequelae. Record the AE/SAE stop date.
- RECOVERED/RESOLVED WITH SEQUELAE – The event persisted and had stabilized without change in the event anticipated. Record the AE/SAE stop date.
- FATAL – A fatal outcome is defined as the SAE that resulted in death. Only the event that was the cause of death should be reported as fatal. AEs/SAEs that were ongoing at the time of death; however, were not the cause of death, will be recorded as "resolved" at the time of death.
- NOT RECOVERED/NOT RESOLVED (ONGOING) – An ongoing AE/SAE is defined as the event was ongoing with an undetermined outcome.
- An ongoing outcome will require follow-up by the site in order to determine the final outcome of the AE/SAE.

- The outcome of an ongoing event at the time of death that was not the cause of death, will be updated and recorded as "resolved" with the date of death recorded as the stop date.
- UNKNOWN – An unknown outcome is defined as an inability to access the participant or the participant's records to determine the outcome (for example, a participant that was lost to follow-up).

All clinically significant abnormalities of clinical laboratory measurements or adverse events occurring during the study and continuing at study termination should be followed by the participant's physician and evaluated with additional tests (if necessary) until diagnosis of the underlying cause, or resolution. Follow-up information should be recorded on source documents.

If any reported adverse events are present when a participant completes the study, or if a participant is withdrawn from the study due to an adverse event, the participant will be contacted for re-evaluation within 2 weeks. If the adverse event has not resolved, additional follow-up will be performed as appropriate. Every effort should be made by the Investigator or delegate to contact the participant until the adverse event has resolved or stabilized.

11.8 Reportable Device Issues

All UADEs, ADEs, device complaints, and device malfunctions will be reported irrespective of whether an adverse event occurred, except in the following circumstances.

The following device issues are anticipated and will not be reported but will reported as an Adverse Event if the criteria for AE reporting described above are met:

- Component disconnections
- CGM sensors lasting fewer than the number of days expected per CGM labelling
- CGM tape adherence issues
- Pump infusion set occlusion not leading to ketosis
- Battery lifespan deficiency due to inadequate charging or extensive wireless communication
- Intermittent device component disconnections/communication failures not leading to system replacement
- Device issues clearly addressed in the user guide manual that do not require additional troubleshooting
- Skin reactions from CGM sensor placement or pump infusion set placement that do not meet criteria for AE reporting

11.9 Timing of Event Reporting

- UADEs must be reported within 10 working days to the FDA after the sponsor first receives notice of the adverse effect.
- Other reportable adverse events, device malfunctions (with or without an adverse event) and device complaints should be reported promptly, but there is no formal required reporting period.

- The IDE Sponsor will investigate the UADE and if indicated, report the results of the investigation to the IRBs, FDA, and DSMB within 10 working days of the study team becoming aware of the UADE per 21CFR 812.46(b) (2).
- The Medical Monitor will determine if the UADE presents an unreasonable risk to participants. If so, the DSMB must ensure that all investigations, or parts of investigations presenting that risk, are terminated as soon as possible but no later than 5 working days after the Medical Monitor makes this determination and no later than 15 working days after first receipt notice of the UADE.
- In the case of a device system component malfunction (e.g. pump, CGM, control algorithm), information will be forwarded to the responsible manufacturer by the study personnel.

11.10 Stopping Criteria

11.10.1 Participant Discontinuation

Rules for discontinuing study device use are described below.

- The investigator believes it is unsafe for the participant to continue the intervention. This could be due to the development of a new medical condition or worsening of an existing condition; or participant behaviour contrary to the indications for use of the device that imposes on the participant's safety
- The participant requests that the treatment be stopped
- The participant tests positive for COVID-19 (during study testing or otherwise within 14 days of study start) or subsequently develops symptoms for COVID-19 and tests positive.
- Diagnosis of DKA. Any severe hypoglycemia event meeting the definition in section 11.2.1 of the protocol.

11.10.2 Suspending/Stopping Overall Study

In the case of an unanticipated system malfunction resulting in a severe hypoglycemia or severe hyperglycemia event (as defined in section 11.2.2), use of the study device system will be suspended while the problem is diagnosed.

In the event that two distinct episodes of DKA or two distinct severe hypoglycemia events as defined in section 11.2 occur, the overall study would be suspended while the underlying conditions are determined.

In addition, study activities could be similarly suspended if the manufacturer of any constituent study device requires stoppage of device use for safety reasons (e.g. product recall). The affected study activities may resume if the underlying problem can be corrected by a protocol or system modification that will not invalidate the results obtained prior to suspension. The study Medical Monitor will review all adverse events and adverse device events that are reported during the study and will review compiled safety data at periodic intervals . The Medical Monitor may request suspension of study activities or stoppage of the study if deemed necessary based on the totality of safety data available.

11.11 Independent Safety Oversight

A Medical Monitor will review all DKA and severe hypoglycemia irrespective of relatedness to study device use, and all serious events (including UADEs) related to study device use at the time of occurrence. The Medical Monitor can request modifications to the study protocol or suspension or outright stoppage of the study if deemed necessary based on the totality of safety data available. Details regarding Medical Monitor review will be documented in a separate Medical Monitor document.

11.12 Definition of a Data Breach

A data breach is defined in the HITECH Act (43 USC 17932) as an unauthorized acquisition, access, or use of protected health information (PHI) that compromises the security or privacy of such information.

Chapter 12 Miscellaneous Considerations

12.1 Prohibited Medications, Treatments, and Procedures

Participants using glulisine at the time of enrollment will be asked to contact their personal physician to change their prescribed personal insulin to lispro or aspart for the duration of the trial.

The study devices (study insulin pump, study CGM) must be removed before Magnetic Resonance Imaging (MRI), Computed Tomography (CT) or diathermy treatment. Participants may continue in the trial after temporarily discontinuing use if requiring one of the treatments above.

12.2 Participant Withdrawal

Participation in the study is voluntary. Participant may withdraw at any time. For participants who do withdraw from the study, the study team will determine if their data will be used in analysis.

12.3 Confidentiality

For security and confidentiality purposes, subjects will be assigned an identifier that will be used instead of their name. Protected health information gathered for this study may be shared with the third-party collaborators. De-identified subject information may also be provided to collaborators involved in the study after the appropriate research agreement has been executed.

Chapter 13 Statistical Consideration

13.1 Design and Randomization

The main study is itself an early exploratory study to assess glycemic responses of a fully closed-loop system (Rocket AP). This information is detailed in Table 1.

Randomization will occur via selection from the above list using permuted blocks in groups of 4.

13.1.1 Planned Analysis

Our primary objective is to assess the impact of priming bolus on post prandial FCL control therefore we will test the following statistical hypotheses

a. Null Hypothesis: There is no difference in the means of time spent in the 70-180mg/dL range during daytime between FCL with and without prandial priming bolus (BPS at 6% and 0% of TDI respectively)

b. Alternative Hypothesis: There is a difference in the means of time spent in the 70-180mg/dL range during daytime between FCL with and without prandial priming bolus (BPS at 6% and 0% of TDI respectively)

To do so we will use repeated measure ANOVA models to predict daytime time in range with the BPS status a fixed effect and baseline HbA1c and gender as covariates.

Secondary outcomes:

All secondary outcomes will be similarly analyzed. If an outcomes distribution is not suited for mixed model analysis (e.g. profound skewness, or large atom at boundary) we will perform paired Wilcoxon signed rank test (and loose the capacity to use covariate) to test difference in the median instead of the mean; this is expected for time below 70mg/dL, number of hypoglycemia, and possibly time above 250mg/dL.

We do not plan to correct for multiple comparisons.

We do not expect substantial missing values in this highly supervised study, but if more than 3 subjects have one or more missing admissions, we will consider switching from RANOVA to mixed model repeated measures.

13.2 Sample Size

As a early exploratory Study, the goal will be to complete up to 20 participants in the main study to provide data from a variety of individuals. This number was chosen out of feasibility and not from a formal power calculation. (The Pilot Study for this proposal will assess ease of system and will be completed in a minimum of 2-3 individuals prior to the beginning of the Main Study.) With N=20 and our randomized crossover design (allowing for paired comparison), we can hope to detect a minimum effect size of 0.66 at a power of 80%. Based of prior FCL study, the standard deviation of daytime TIR is approximately 12%, leading to a detectable difference in daytime TIR of 8%.

13.3 Outcome Measures

13.3.1 Primary Efficacy Endpoint

The study design allows for multiple comparisons of blood glucose control during the study meals and exercise sessions, with for the primary comparison of interest being between the RocketAP with and without BPS. Our primary endpoint is CGM time-in-range 70-180 mg/dL for the daytime period 6 am – 12 am when on each treatment modality (BPS vs. no BPS).

13.3.2 Secondary Outcomes

Each admission is separated into windows of analysis:

- The entirety of the admission (24h: 4pm to 4pm)
- The 4 hours following each of the meals.
- The overnight period (12 am to 6 am)

For each of these periods we will compute the following outcomes:

- Number of hypoglycemia events defined as at least two consecutive CGM values <70mg/dL or a hypoglycemia treatment (two events separated by less than 30 minutes are counted as one).
- Percent CGM time <70 mg/dL
- Percent CGM time between 80-140mg/dL
- Percent CGM time between 70-180mg/dL
- Percent CGM time >180 mg/dL
- Percent CGM time >250 mg/dL
- Units of insulin injected
- Area under the curve when accounting for starting BG
- Low Blood Glucose Index
- High Blood Glucose Index
- CGM coefficient of variation
- Mean CGM

13.3.3 CGM data treatment

- Saturated CGM values "High" and "Low" will be replaced by 401mg/dL and 39mg/dL respectively.
- Any CGM gaps shorter than 1 hour will be interpolated
- CGM data during recorded occlusion event will be removed from analysis as follow: any measurement less than 2h before or after the time of record will be removed.
- CGM data following a pump/DiAs communication interruption >1h by less than 2h will be removed

13.3.4 Outcome computation conditions

Outcomes will only be computed if at least 80% of the analysis window CGM measurements (after data treatment) are available

13.4 Safety Analyses

We will assess for the system's functionality, including the ability of the system to run its code without error (delivering insulin safely, as planned), as well as its ability to avoid low BG <70 mg/dL.

13.5 Baseline Descriptive Statistics

Baseline demographic and clinical characteristics of the cohort of all randomized participants will be summarized in a table using summary statistics appropriate to the distribution of each variable. Descriptive statistics will be displayed overall and by treatment group.

Will include:

- Age
- HbA1c
- Gender
- Race/ethnicity
- CGM use before enrollment
- AID use before enrollment
- Diabetes duration
- BMI
- Total Daily Insulin

13.6 Device Issues

The following tabulations and analyses will be performed during time on the UVa AP systems to assess device issues:

- Device malfunctions requiring study team contact and other reported device issues
- % time CGM data available
- % time with closed loop control

Chapter 14 Data Collection and Monitoring

14.1 Case Report Forms and Device Data

The study data are collected through a combination of case report forms (electronic and paper) and electronic device data files obtained from the software and individual hardware components. These electronic device files and electronic CRFs are considered the primary source documentation.

When data are directly collected in electronic case report forms, this will be considered the source data. Records will be maintained in accordance with ICH E6 and institutional regulatory requirements for the protection of confidentiality of participants.

14.2 Study Records Retention

Study documents should be retained for a minimum of 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

14.3 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, Good Clinical Practices (GCP), or procedure requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. As a result of deviations, corrective actions may be developed by the site and implemented as appropriate. Major deviations will be reported to the IRB-HSR within 7 calendar days of when the study team becomes aware of the event.

Chapter 15 Ethics/Protection of Human Participants

15.1 Ethics Standard

The investigator will ensure that this study is conducted in full conformity with Regulations for the Protection of Human Participants of Research codified in 45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and/or the ICH E6.

15.2 Institutional Review Boards

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form will be IRB approved; a determination will be made regarding whether previously consented participants need to be re-consented.

15.3 Informed Consent Process

15.3.1 Consent Procedures and Documentation

Informed consent is a process that is initiated prior to an individual's agreement to participate in the study and continues throughout the individual's study participation. Extensive discussion of risks and possible benefits of participation will be provided. Consent forms will be IRB approved and the participant will be asked to read and review the document. The investigator or their delegate will explain the research study to the participant and answer any questions that may arise. All participants will receive a verbal explanation in terms suited to their comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participant will have the opportunity to carefully review the written consent form and ask questions prior to signing.

The consenting process will involve discussing the study at length in a phone call/HIPAA compliant telecommunication method for consenting that is not face to face. The participant will sign the informed consent document prior to any procedures being done specifically for the study. The consent form may be signed electronically with the use of the Part 11 compliant version of DocuSign for both in-person and telecommunication screening visits. The study team will follow the FDA part 11 compliant process of verification of reviewing two forms of identification if signing electronically off site. A HIPAA compliant video conferencing tool will be utilized during the consenting process of the telecommunication screening visit to facilitate review of the participant's identification. A copy of the informed consent document will be given to the participant for their records. The rights and welfare of the participants will be protected by

emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

15.3.2 Participant and Data Confidentiality

The study monitor, representatives of the IRB or device company supplying study product may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the participants in this study.

The study participant's contact information will be securely stored at the clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by local IRB and Institutional regulations.

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The study participant's contact information will be securely stored at the clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by local IRB and Institutional regulations.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the University of Virginia Center for Diabetes Technology. The study data entry and study management systems used by research staff will be secured and password protected. At the end of the study, all study databases may be de-identified and archived at the University of Virginia Center for Diabetes Technology.

Chapter 16 References

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