Signature Page

Control-IQ Technology for High Insulin Users with Type 1 Diabetes (Higher-IQ)

Protocol Identifying Number: TP-0009856

IDE Number: G210300

IDE Sponsor: Tandem Diabetes Care, Inc.

Version Number: v 5.0

21 MAR 2022

Medical Monitor and Protocol Chair	
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Name, degree **Title**	Ravid Sasson-Katchalski, PhD Associate Director, Clinical Affairs, Tandem Diabetes Care
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Protocol Revision History

Version Number	Amendment Date	Brief Description of Changes
1.0	12 OCT 2021	Initial Version Submitted to FDA
2.0	10 NOV 2021	First Version Approved by FDA
3.0	18 JAN 2022	• Added IDE number to cover page • Added protocol revision history table • Clarified Stats Analysis Plan endpoints, with detailed description of time periods for meal and exercise challenge analysis • Clarified sponsor responsibilities in AE/device issue reporting • Clarified exercise/meal challenge instructions • Removed SUSAR and other definitions not related to this trial, as investigational insulin will not be used • Clarified the sponsor's Medical Director will serve as the Medical Monitor • Other minor clarifications on wording for consistency throughout the protocol
4.0	01 MAR 2022	• Clarified participant will plan to use at least one basal rate > 3 units/hr with the study pump. • Clarified participants using SGLT-2 inhibitors, GLP-1 analogs, or other non-insulin glucose medications other than metformin must be on a stable dose over the last 3 months prior to enrollment. • Clarified abnormal screening electrocardiogram consistent with increased risk during study exercise activities, and that investigator will review all electrocardiograms. • Clarified procedures for verifying subject identifiers. • Added to section 7.1 that Humalog or Novolog will be provided to participants. • Clarified details of monitoring plan, and specific data that would be considered source material that could be monitored. • Other minor clarifications on wording for consistency throughout the protocol.
5.0	21 MAR 2022	• Added Special Considerations for Participants Taking SGLT-2 inhibitors, GLP-1 Receptor Agonists, or DPP-IV Inhibitors to add scheduled ketone checks for participants using SGLT-2 inhibitors, when to stop

		SGLT-2 inhibitors, and updated hyperglycemia treatment guidelines. • Updated exclusion criteria to address adjuvant medication use of glucose lowering agents and weight loss agents. • Updated prohibited medications. • Updated section 6.6.1 discontinuation of study device. • Updated inclusion criteria to note goal enrollment of at least 25% of participants using a basal rate above 3 units/hr for substantially all day • Added definition of euglycemic DKA.

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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
ADE	Adverse Device Effect
AE	Adverse Event
AID	Automated Insulin Delivery
BGM	Blood Glucose Meter
BMI	Body Mass Index
CFR	Code of Federal Regulations
CGM	Continuous Glucose Monitoring
CLC	Closed-Loop Control
DCCT	Diabetes Control & Complications Trial
DKA	Diabetic Ketoacidosis
eCRF	Electronic Case Report Form
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HbA1c	Hemoglobin A1c
ICF	Informed consent form
ICH	International Conference of Harmonisation
IDE	Investigational Device Exemption
IRB	Institutional Review Board
RBM	Risk-Based Monitoring
SAE	Serious Adverse Event
T1D	Type 1 Diabetes
UADE	Unanticipated Adverse Device Effect

Site Principal Investigator Statement of Compliance

Protocol Identifying Number:	TP-0009856
Protocol Name:	Control-IQ Technology for High Insulin Users with Type 1 Diabetes (Higher-IQ)
Protocol Version / Date:	5.0 / 21 MAR 2022

The Principal Investigators (undersigned) hereby declare that they have read this protocol and agree to its contents.

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

By written consent to this protocol, the investigators agree to the above and to fully co-operate with all monitoring and audits in relation to this trial by allowing direct access to all documentation, including source data, by authorized individuals representing Tandem Diabetes Care, Inc., IRBs and/or by the US Federal, State and local regulatory authorities.

Investigator Name: _____

Investigator Signature: _____

Date (DD/MMM/YYYY): _____

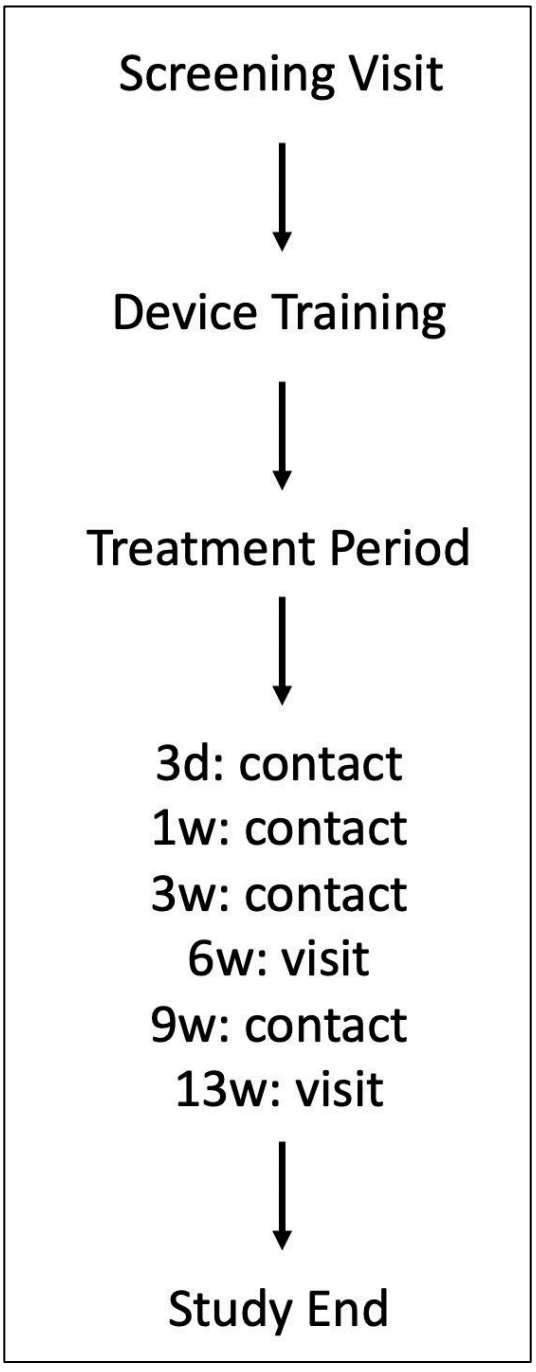
PROTOCOL SUMMARY

Study Sponsor	Tandem Diabetes Care, Inc.
Protocol Number	TP-0009856
Protocol Title	Control-IQ Technology for High Insulin Users with Type 1 Diabetes (Higher-IQ)
Précis	A prospective, single-arm study of 13 weeks of home use of the Control-IQ automated insulin delivery (AID) system in individuals with type 1 diabetes who will plan to use at least one basal rate > 3 units/hr, age 18 and older. Subjects will use the Control-IQ 1.5 System. Exercise and meal challenges will be performed during the study.
Products	t:slim X2 insulin pump with Control-IQ technology v1.5 (Control-IQ System)
Objectives	The objectives of the study are to assess safety and explore glycemic outcomes with use of an automated insulin delivery (AID) system (t:slim X2 with Control-IQ Technology v1.5) in adults with type 1 diabetes who will plan to use at least one basal rate > 3 units/hr.
Number of Sites	Up to 5 clinical sites in the US.
Study Design	Existing insulin pump users (to include AID users) will use the study system (pump and CGM) in closed-loop mode for 13 weeks.
Number of Participants	Up to 60 adults with type 1 diabetes may be screened, so at least 30 finish closed-loop use.
Participant Population:	**Eligibility to enroll in the study will be assessed based on the following inclusion criteria:** 1. Age ≥ 18 years 2. Diagnosis of type 1 diabetes for at least 1 year 3. Currently using an insulin pump (of any brand) for at least 3 months, and will plan to use at least one basal rate above 3 units/hr with the study pump a. *Goal is at least 25% of study participants are on a basal rate above 3 units/hr for substantially all day* 4. HbA1c < 10.5% 5. Weight ≤ 200 kg 6. Residing full-time in the United States, with no anticipated travel outside the United States during the period of study participation. 7. Participant has agreed to participate in the study; and has read, understood and signed the informed consent form (ICF); and has agreed to follow all study procedures, including suspending use of any personal CGM for the duration of the clinical trial once the study CGM is in use. 8. Willing to use only aspart (novolog) or lispro (humalog) insulin with the study pump, with no use of concentrated insulin above U-100, long-acting basal insulin injections, or inhaled insulin with the study pump 9. Have current glucagon product to treat severe hypoglycemia (injectable or nasal) at home (will provide prescription if they do not have one) 10. Willing and able to perform the study exercise and meal challenges. 11. Have a care partner, trained in hypoglycemia and hyperglycemia treatment guidelines, present during the challenges and until the next day. 12. Investigator has confidence that the participant can successfully operate all study devices and is capable of adhering to the protocol, including ability to respond to alerts and alarms, and to provide basic diabetes self-management. **Eligibility to enroll in the study will be assessed based on the following exclusion criteria:** 1. More than 1 episode of diabetic ketoacidosis (DKA) in the past 6 months 2. More than 1 episode of severe hypoglycemia (needing assistance) in the past 6 months

	3. Inpatient psychiatric treatment in the past 6 months 4. History of drug abuse (defined as any illicit drug use) or history of alcohol abuse prior to screening or unwillingness to agree to abstain from illicit drugs throughout the study. 5. For Female: Currently pregnant or planning to become pregnant during the time period of study participation • *A negative pregnancy test will be required for all females of child-bearing potential* • *Counseling on appropriate birth control options will be provided to all females of child-bearing potential* 6. Use of sulfonylureas, meglitinides, Symlin or other medications specifically listed in section 7.3 of the protocol or determined by investigator to interfere with the study 7. Unstable dose of SGLT-2 inhibitor, GLP-1 receptor agonist, DPP-IV inhibitor, as listed in section 7.3 of the protocol, or starting a new non-insulin glucose lowering or weight loss agent during the trial 8. Hemophilia or any other bleeding disorder 9. History of heart, liver, lung or kidney disease determined by investigator to interfere with the study 10. History of allergic reaction to Humalog or Novolog 11. Use of glucocorticoids other medications determined by investigator to interfere with study 12. Abnormal screening electrocardiogram consistent with increased risk during study exercise activities, such as arrhythmia, ischemia, or prolonged QTc interval. Investigator will review all electrocardiograms 13. Significant chronic kidney disease (which could impact CGM accuracy in investigator's judgment) or hemodialysis 14. History of adrenal insufficiency 15. History of abnormal TSH consistent with hypothyroidism or hyperthyroidism that is not appropriately treated 16. History of gastroparesis 17. A condition, which in the opinion of the investigator or designee, would put the participant or study at risk 18. Participation in another pharmaceutical or device trial at the time of enrollment or anticipated for during the time period of study participation 19. Employed by, or having immediate family members employed by Tandem Diabetes Care, Inc., or having a direct supervisor at place of employment who is also directly involved in conducting the clinical trial (as a study investigator, coordinator, etc.); or having a first-degree relative who is directly involved in conducting the clinical trial
Participant Duration	Approximately 13-15 weeks.

Study Endpoints	Primary Safety Endpoints: • Severe hypoglycemia (with cognitive impairment such that assistance of another individual is needed for treatment) during study compared with data on severe hypoglycemic events reported by T1D Exchange clinic registry over a 3-month time period • Diabetic ketoacidosis (event rate) • Number of unanticipated adverse device effects • Number of other serious adverse events Secondary Safety Endpoints: • All adverse events • CGM hypoglycemia outcomes ◆ Overall % time <54 mg/dL ◆ Overall % time <70 mg/dL Exploratory: • Times in ranges-overall (70-180 mg/dL, >180 mg/dL, >250 mg/dL, 70-140 mg/dL) • Mean glucose • Overall variability (CV and SD) • HbA1c change from baseline • CGM metrics for hypoglycemia, hyperglycemia, and variability during daytime and nighttime
Protocol Overview/Synopsis	After consent is signed, eligibility will be assessed. <u>Treatment Period</u>: Participants will return to clinic to undergo device training with the study CGM and study pump. Participants will then use the study pump for ~90 days during the study period. Participants will have a phone follow up visit at 3 days, 1 week, 3 weeks, an in clinic visit at 6 weeks, a phone follow up visit at 9 weeks, and a final clinic visit at ~13 weeks. Participants will use the t:slim X2 insulin pump with Control-IQ technology 1.5 turned on. It is acceptable to use manual mode when there is a loss of CGM data. Each participant will perform 3 meal and 3 exercise challenges during the study. An assessment of adverse events, using open ended questions to capture hyperglycemic and hypoglycemic events, and their underlying cause and relationship to the study device or other parts of the system (such as the infusion set), will occur at all visits/contacts. <u>Study Safety Plan</u>: Participants will be given a blood glucose and ketone meter to use throughout the study, and will be trained on their use by qualified staff. BGM readings will be performed in accordance with the study participant instruction sheet and per CGM manufacturer instructions. Ketone readings will be performed per the study participant instruction sheet. Site investigators may adjust insulin delivery profile settings as needed throughout the study in accordance with their clinical practice.

SCHEMATIC OF STUDY DESIGN



SCHEDULE OF STUDY VISITS AND PROCEDURES

	Screening Visit	Control-IQ 1.5 Training Visit	Control-IQ Use						
		Up to 2 weeks after screening	3d	1w	3w	6w	9w	13w[1]	UV
Visit (V) or Contact (C)	**V**	**V**	**C**	**C**	**C**	**V**	**C**	**V**	**V/C**
Informed Consent	**X**								
Eligibility Assessment	**X**								
Medical history/ physical exam	**X**								
Height, weight, blood pressure and pulse	**X**								
HbAlc (POC or local lab)	**X**								
ECG	**X**								
Pregnancy test (females of child-bearing potential)	**X**	**X[2]**							
Assessment of Device Use	**X**								
Study system training		**X**							
HbA1c (Central Lab)		**X**						**X**	
AE Assessment		**X**	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Upload and Review Study Device Data			**X**	**X**	**X**	**X**	**X**	**X**	**X**

[1]End of study visit or upon early withdrawal of the subject from the study. Note, HbA1c (Central Lab) will only be drawn if the subject has reached at least 6 weeks of follow-up.

[2]Pregnancy test does not need to be repeated if screening and Control-IQ training visits are performed on the same day.

Chapter 1: Background Information

1.1 Introduction

1.1.1 Disease Background

Type 1 diabetes affects 1.25 million people in the United States. Approximately 70% of individuals with type 1 diabetes report poor metabolic control, and do not meet the American Diabetes Association's recommended goal of hemoglobin A1c (HbA1c) level of 7.0%. These findings indicate the need for better approaches to type 1 diabetes management.

1.1.2 Tandem X2 Insulin Pump with Control-IQ Technology

The Tandem X2 insulin pump with Control-IQ technology is an FDA-approved closed-loop control (CLC) system based on the control algorithm developed and initially tested in the University of Virginia's DiAs system and then implemented in the inControl system (TypeZero, Technologies, Inc.). Use of the Control-IQ system has been extensively tested in adults and children with type 1 diabetes (T1D), demonstrating its efficacy and safety when used with insulin lispro (Humalog) or insulin aspart (Novolog).[1,2] The system is currently approved for ages 6 years and older and use in younger children is currently being studied (clinical trials.gov NCT04796779). There are over 150,000 users of the system since it became commercially available in 2020. A recent evaluation of real-world use of the system in 9,451 users age $\geq$6 years with at least 12 months of system use found results comparable to those found in the randomized trials.[3]

Since the initial approval of the system, modifications have been made in the software, which is referred to as version 1.5. These modifications include modest usability improvements and other enhancements intended to further reduce risk. The Control-IQ 1.5 system also removes the 3 units/hr basal clipping, allowing the pump to deliver programmed user profile basal rates above 3 units/hr when 30 minute predicted glucose is expected to be in the target range. This has the potential to further improve outcomes in individuals using basal rates at or above this threshold.

1.2 Rationale

The objective of this single-arm, prospective study is to assess safety and explore glycemic outcomes associated with use of the Control-IQ 1.5 system in adults with type 1 diabetes using basal rates > 3 units/hr for at least part of the day.

1.3 Potential Risks and Benefits

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 events.

1.3.1 Known Potential Risks

1.3.1.1 Blood Draw

A venipuncture and/or fingerstick will be performed to obtain blood for HbA1c measurement. Venipuncture can cause 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. A fingerstick frequently causes transient pain and there may be a small, localized bruise, which may be followed by a small scar that may persist for several weeks. The risk of local infection is less than 1 in 1000 with either venipuncture or fingerstick.

1.3.1.2 CGM and Pump Catheter Risks

There is a small risk of bleeding where the sensor or infusion set is inserted. There is a small risk for developing a local skin infection at the site of CGM sensor placement of pump infusion set placement. This may be associated with swelling, redness and pain; and may require antibiotic therapy. Rarely, a CGM sensor may break and leave a small portion of the sensor under the skin that may cause redness, swelling or pain at the insertion site.

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.

1.3.1.3 Hypoglycemia

As with any person having type 1 diabetes and using insulin, there is always a risk of having 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. 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.

1.3.1.4 Risk of Hyperglycemia

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.

1.3.1.5 Risk of Device Reuse

All devices will be used by a single study participant only. There will be no device reuse.

1.3.1.6 Potential Risks of the CLC System

Even though the study system has been tested prior to this study, there is still a risk that parts of the system may not function properly. The following are possible reasons the system may deliver too much insulin or incorrectly stop insulin delivery:

- CGM sensor reads higher or lower than the actual glucose level which increases risk for hypoglycemia and hyperglycemia with automated insulin delivery system;
- Device malfunctions that could produce a suspension of insulin delivery or over delivery of insulin.

1.3.1.7 Other Risks

Data downloaded from the study CGM and study pump will be collected for the study. The downloaded data from the participant's home pump and CGM (if available) at the screening visit will include data from prior to the date of the screening visit and will include data from the period beyond the last 2 weeks prior to screening. Some people may be uncomfortable with the researchers' having such detailed information about their daily diabetes habits.

1.3.2 Benefits

Participants may achieve better glucose control than they are currently achieving using their home insulin pump.

The individual participant may not benefit from study participation.

1.3.3 Risk Assessment

Based on the facts that (1) individuals with diabetes experience mild hypoglycemia and hyperglycemia frequently as a consequence of the disease and its management, (2), 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 (3) rapid reversal of hypoglycemia and hyperglycemia can be achieved, it is the assessment of the Sponsor that this protocol is an investigation involving a minor increase over minimal risk. In addition, it is the belief of the Sponsor that this study also presents prospect of direct benefit to the participants and general benefit to others with diabetes.

1.4 General Considerations

The study is being conducted in compliance 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).

There is no restriction on the number of participants to be enrolled by each clinical center toward the overall recruitment goal.

In accordance with 21 CFR 812.66, the protocol is considered a significant risk device study, due to the fact that the intervention is investigational. Therefore, an investigational device exemption (IDE) from the U.S. Food and Drug Administration (FDA) is required to conduct the study.

Chapter 2: Study Enrollment and Lead-in Period

2.1 Participant Recruitment and Enrollment

Enrollment will proceed with the goal of having up to 60 subjects screened, so that at least 30 complete closed loop use.

Study participants will be recruited from up to 5 clinical centers in the United States without regard to gender, race, or ethnicity. There is no restriction on the number of participants to be enrolled by each site toward the overall recruitment goal.

2.1.1 Informed Consent and Authorization Procedures

Potential eligibility may be assessed as part of a routine-care examination. Before completing any procedures or collecting any data that are not part of usual care, written or electronic informed consent will be obtained.

For potential study participants, the study protocol will be discussed with the potential study participant by study staff. The potential study participant will be given the Informed Consent Form to read. Potential study participants will be encouraged to discuss the study with family members and their personal physicians(s) before deciding whether to participate in the study.

A copy of the consent form will be provided to the participant, and a copy will be added to the participant's study record.

As part of the informed consent process, each participant will be asked to sign an authorization for release of personal information. The investigator, or his or her designee, will review the study-specific information that will be collected and to whom that information will be disclosed. After speaking with the participant, questions will be answered about the details regarding authorization.

A participant is considered enrolled when the informed consent form has been signed.

2.2 Participant Eligibility Criteria

2.2.1 Inclusion Criteria

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

1. Age ≥ 18 years
2. Diagnosis of type 1 diabetes for at least 1 year
3. Currently using an insulin pump (of any brand) for at least 3 months, and will plan to use at least one basal rate above 3 units/hr with the study pump
    a. *Goal is at least 25% of study participants are on a basal rate above 3 units/hr for substantially all day*
4. HbA1c < 10.5%
5. Weight ≤ 200 kg
6. Residing full-time in the United States, with no anticipated travel outside the United States during the period of study participation.
7. Participant has agreed to participate in the study; and has read, understood and signed the informed consent form (ICF); and has agreed to follow all study procedures, including

suspending use of any personal CGM for the duration of the clinical trial once the study CGM is in use.

8. Willing to use only aspart (novolog) or lispro (humalog) insulin with the study pump, with no use of concentrated insulin above U-100, long-acting basal insulin injections, or inhaled insulin with the study pump.
9. Have current glucagon product to treat severe hypoglycemia (injectable or nasal) at home (will provide prescription if they do not have one)
10. Willing and able to perform the study exercise and meal challenges.
11. Have a care partner, trained in hypoglycemia and hyperglycemia treatment guidelines, present during the challenges and until the next day.
12. Investigator has confidence that the participant can successfully operate all study devices and is capable of adhering to the protocol, including ability to respond to alerts and alarms, and to provide basic diabetes self-management.

2.2.2 Exclusion Criteria

Individuals meeting any of the following exclusion criteria at baseline will be excluded from study participation.

1. More than 1 episode of diabetic ketoacidosis (DKA) in the past 6 months
2. More than 1 episode of severe hypoglycemia (needing assistance) in the past 6 months
3. Inpatient psychiatric treatment in the past 6 months
4. History of drug abuse (defined as any illicit drug use) or history of alcohol abuse prior to screening or unwillingness to agree to abstain from illicit drugs throughout the study.
5. For Female: Currently pregnant or planning to become pregnant during the time period of study participation
   - *A negative pregnancy test will be required for all females of child-bearing potential*
   - *Counseling on appropriate birth control options will be provided to all females of child-bearing potential*
6. Use of sulfonylureas, meglitinides or other medications specifically listed in section 7.3 of the protocol or determined by investigator to interfere with the study
7. Unstable dose of SGLT-2 inhibitor, GLP-1 receptor agonist, or DPP-4 inhibitor as listed in section 7.3 of the protocol, or starting a new non-insulin glucose lowering or weight loss agent during the trial
8. Hemophilia or any other bleeding disorder
9. History of heart, liver, lung or kidney disease determined by investigator to interfere with the study
10. History of allergic reaction to Humalog or Novolog
11. Use of glucocorticoids or other medications determined by investigator to interfere with study
12. Abnormal screening electrocardiogram consistent with increased risk during study exercise activities, such as arrhythmia, ischemia, or prolonged QTc interval. Investigator will review all electrocardiograms

13. Significant chronic kidney disease (which could impact CGM accuracy in investigator's judgment) or hemodialysis
14. History of adrenal insufficiency
15. History of abnormal TSH consistent with hypothyroidism or hyperthyroidism that is not appropriately treated
16. History of gastroparesis
17. A condition, which in the opinion of the investigator or designee, would put the participant or study at risk
18. Participation in another pharmaceutical or device trial at the time of enrollment or anticipated for during the time period of study participation
19. Employed by, or having immediate family members employed by Tandem Diabetes Care, Inc., or having a direct supervisor at place of employment who is also directly involved in conducting the clinical trial (as a study investigator, coordinator, etc.); or having a first-degree relative who is directly involved in conducting the clinical trial

2.3 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 study personnel and local laboratory testing if needed to screen for exclusionary medical conditions.

2.3.1 Data Collection and Testing

A standard physical exam (including vital signs and height and weight measurements) will be performed by the study investigator or designee (a physician, fellow, nurse practitioner or a physician assistant). Height, weight and vital signs may be recorded by appropriately delegated office staff.

The following procedures will be performed/data collected/eligibility criteria checked and documented:

- Inclusion and exclusion criteria assessed
- Demographics (age, sex, race and ethnicity and socioeconomic information)
- Subject initials to verify downloaded device data and eCRF entry is associated with the correct individual
- Contact information (retained at the site and not entered into study database)
- Medical history
- Substance use history (drinking, smoking, and drug habits)
- Concomitant medications
- Physical examination to include:
    - Weight, height
    - Vital signs including measurement of blood pressure and pulse
- Blood draw (venipuncture or fingerstick) for local HbA1c measurement
- Urine pregnancy test for all females who are premenopausal and not surgically sterile
- ECG performed at screening for all participants

- Current device download, to include insulin pump and CGM device data, for up to the last 90 days of data

Screening procedures will last approximately 1-2 hours. The screening visit must occur in clinic and cannot be performed remotely.

2.4 Screen Failures

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

Chapter 3: Treatment Period

3.1 Control-IQ 1.5 Training Visit

After screening, participants will have a clinic visit at which they will undergo CGM and study pump device training.

The device training visit should be completed within 2 weeks of screening, and may be performed the same day as the screening visit. If not completed within 2 weeks of screening, re-review of screening results by the investigator should be performed, who may ask for repeated testing as per investigator judgement. The device training visit may be extended over the course of more than 1 session if needed. The device training visit must occur in clinic and cannot be performed remotely.

A blood sample (venipuncture or fingerstick) will be obtained to send to the central laboratory for HbA1c measurement.

A urine pregnancy test for all females who are premenopausal and not surgically sterile will be completed.

Participants will receive supplies for blood glucose and ketone testing. Quality Control (QC) testing will be performed on the meters before they are dispensed.

As all study participants are existing pump users (of any brand pump), pump settings will be transferred over from the participant's current pump. The study investigator may then further adjust insulin delivery profile settings as clinically indicated.

3.1.1 Training on System Use

All participants will receive study system training from a qualified trainer.

At a minimum training will include the following:

- Calibration of the CGM in accordance with manufacturer labeling
- Procedures for treating severe hypoglycemia
- Procedures for identifying potential infusion set failure and steps to take including the checking of the blood ketone level and changing the infusion set

The participant will be given a User Guide as a reference as well as Hypoglycemia and Hyperglycemia Treatment Guidelines as part of the Study Participant Instruction Sheet.

Participants will be instructed to download the study device prior to each phone contact or office visit.

The participant will be instructed to use the system in closed-loop mode except 1) when no calibrated CGM sensor is available or 2) 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, participant will be instructed to turn off Control-IQ for approximately four hours.

The participant will also be instructed to contact study staff during periods of illness with an elevated temperature >101.5 degrees Fahrenheit (38.6 degrees Celsius), periods of significant illness, or during periods of use of medications such as epinephrine for the emergency treatment of a severe allergic reaction or asthma attack in addition to use of oral or injectable glucocorticoids to determine if closed-loop use should be temporarily discontinued.

Participants taking SGLT-2 inhibitors will be instructed to discontinue use of their SGLT-2 inhibitor during times of illness where they are at higher risk to develop ketones, to include temperature >101.5

degrees Fahrenheit (38.6 degrees Celsius), any gastrointestinal illness, dehydration, decreased PO intake, fasting, or periods of significant illness.

Participants will be provided with contact information and will be asked to call the study clinical staff for any health-related issues and for technical issues with the system. Participants may use the study pump without Control-IQ activated and study CGM during periods of component disconnections or technical difficulties.

Participants may use available manufacturer-provided CGM software and features of the study CGM related to mobile data access or remote monitoring, but will be instructed not to use any third-party components for this purpose. The t:connect mobile app from Tandem Diabetes Care will not be available for use during the trial, and will not pair to the study pump.

Study staff will discuss with the participant that routine contact is required as per the study visit schedule and will make arrangements with the participant for the contacts. If the participant cannot be reached, the participant's other contact methods will be utilized, including the emergency contact. Participants who are not compliant with the arranged contacts on two separate occasions may be discontinued at the discretion of the investigator.

Participants will be instructed that they must have a care partner, trained in the study hypoglycemia and hyperglycemia treatment guidelines, present during the study meal and exercise challenges, and present overnight after the challenges. These hypoglycemia and hyperglycemia treatment guidelines will be reviewed with the care partner prior to initiating any challenges.

Following the Control-IQ 1.5 Training Visit, participants will use the study pump for ~90 days during the Treatment Period.

3.1.2 Training on Management of Hypoglycemia

The t:slim X2 with Control-IQ system will issue a predictive hypoglycemia alert (Control-IQ Low Alert) when the system predicts BG <70 mg/dL within the next 15 minutes (<80 mg/dL when exercise mode is activated). Participants will be permitted to change the CGM low glucose threshold alert setting on their device or mobile app, but will be instructed to choose a value no less than 70 mg/dL.

If the participant receives a Control-IQ Low Alert, a message appears on the user interface that is accompanied by vibration followed by vibrations and/or sound if not acknowledged by the user in 5 minutes. This alert remains on the screen until acknowledged by the participant. The user is prompted to test blood glucose and treat with carbohydrate.

Participants on GLP-1 receptor agonists and DPP-4 inhibitors will be reminded to carefully monitor post prandial blood sugars, as use of GLP-1 receptor agonists can have lower blood glucose levels after meals.

The participant and companion if available will be instructed that if severe hypoglycemia occurs, the study pump's insulin delivery should be suspended and glucagon administration if the participant is unable to consume carbohydrate.

Participants will be required to have a home glucagon emergency kit. Participants who currently do not have one will be given a prescription for the glucagon emergency kit.

3.1.3 Training on Management of Hyperglycemia

The t:slim X2 with Control-IQ system will issue a predictive hyperglycemia alert (Control-IQ High Alert) when the system has increased insulin delivery, but detects a CGM value above 200 mg/dL and does not predict the value will decrease in the next 30 minutes. During the course of the study, participants will be permitted to change the CGM high glucose threshold alert setting on their device or mobile app, but will be instructed to choose a value no greater than 300 mg/dL.

If the participant receives a Control-IQ High Alert, a prompt appears on the user interface to check the site for occlusion and test blood glucose.

If a participant's CGM reading is >300 mg/dL for more than 60 minutes or is ≥400 mg/dL at any point, the participant will be instructed to take the following steps:

- Perform a blood glucose meter check.
- If the blood glucose is >300 mg/dL, check for blood ketones with the study ketone meter.
- If the ketone level is ≥ 0.6 mmol/L (or ≥ 2.5 mmol\L at any time), take correction insulin, change insulin (pump) infusion site and contact study staff. Continue to monitor their glucose and blood ketone levels until they return to normoglycemia and ketones are < 0.6 mmol/l.
    - If ketones are <0.6 mmol/l, they will be advised to continue to monitor their glucose until it returns to normoglycemia and to repeat the ketone measurement in 90 minutes if necessary
- If correction insulin is administered via insulin syringe, turn Control-IQ off for four hours and until glucose level has returned to <180 mg/dL.

Special Considerations for Participants Taking SGLT-2 inhibitors, GLP-1 Receptor Agonists, or DPP-IV Inhibitors

Participants taking any SGLT-2 inhibitor will be instructed to perform scheduled ketone checks at least twice a day (morning and evening) during the first two weeks of study device use, and at least once a day thereafter. If a participant taking an SGLT-2 inhibitor develop ketones > 0.6 on two successive occasions during these 2 weeks (the first testing upon waking in a fasted state), they will be withdrawn from the study.

For participants taking any SGLT-2 inhibitor, GLP-1 Receptor Agonist, or DPP-4 inhibitor, if a participant's CGM reading is >250 mg/dL for more than 60 minutes or is ≥400 mg/dL at any point, the participant will be instructed to take the following steps:

- Perform a blood glucose meter check.
- If the blood glucose is >250 mg/dL, check for blood ketones with the study ketone meter.
- If the ketone level is ≥ 0.6 mmol/L (or ≥ 2.5 mmol\L at any time), take correction insulin, change insulin (pump) infusion site and contact study staff. Continue to monitor their glucose and blood ketone levels until they return to normoglycemia and ketones are < 0.6 mmol/l.
    - If ketones are <0.6 mmol/l, they will be advised to continue to monitor their glucose until it returns to normoglycemia and to repeat the ketone measurement in 90 minutes if necessary
- If correction insulin is administered via insulin syringe, turn Control-IQ off for four hours and until glucose level has returned to <180 mg/dL.

3.1.4 Adjustments in Insulin Pump Settings

Insulin and glucose data from the screening visit, as well as follow up visits, will be reviewed and the site investigator may adjust insulin delivery profile settings as needed in accordance with their clinical practice.

3.2 Study Visits and Phone Contacts

Participants will have a phone (or video-conference) follow-up visit at 3 days, 1 week and 3 weeks, a clinic follow-up visit at 6 weeks, a phone follow-up visit at 9 weeks, and a final clinic visit at 13 weeks, within the windows specified below.

TARGET DAY/WEEK	VISIT OR PHONE	TARGET WINDOW (AROUND TARGET DAY/WEEK)
3 days	P	±1 day
1 week	P	±2 days
3 weeks	P	±7 days
6 weeks	V	±7 days
9 weeks	P	±7 days
13 weeks	V	91-98 days

If necessary, visits should be completed out-of-window rather than missed. A visit is not considered missed until the next visit/phone window opens.

The goal will be for all participants to complete all scheduled visits. However, participants who (because of unforeseen circumstances or due to changes in contact precautions that may be needed during the evolving COVID-19 pandemic) are unable or unwilling to return for all follow-up visits will be permitted to return for key visits only (screening visit, device training visit) as an alternative to withdrawal from the study. Remote (phone) visits will still be performed as scheduled. When a participant is placed into this status, remote visits will not be recorded as protocol deviations.

Additional phone and office visits may occur as needed.

For the 6 and 13 week visits, if a clinical site believes these visits need to be performed remotely, the following approvals must be obtained prior to conducting the visit remotely:

- Sponsor approval for the reason the visit cannot be performed in person
- Investigator approval at the site level for the reason the visit cannot be performed in person

In addition, all study procedures listed in section 3.2.1 are to be completed, including upload of the study device and review of the device data. If the final visit is performed remotely, participant will mail in the A1c kit from home and mail back the study devices to the study site.

3.2.1 Procedures at Study Visits

The following procedures will be performed at each visit, unless otherwise specified:

- Review of study device data
- Assessment of compliance with study device use by review of any available device data
- Assessment of device issues that have occurred
- Assessment of adverse events, using open ended questions to capture hyperglycemic and hypoglycemic events, and their underlying cause and relationship to the study device or other parts of the system (such as the infusion set).

At 13 weeks (or if at subject withdrawal), the study staff will then supervise the participants transition back to their standard of care therapy as follows:

- Study staff will re-evaluate the subject's baseline therapy doses, noting changes in basal rates, carbohydrate ratios, and correction factors in use at the end of the trial.

- The study investigator will supervise and confirm the entry of settings in the insulin delivery profile of the participant's home pump at the end of the study.

- Blood draw (venipuncture or fingerstick) for HbA1c measurement at central lab (Device Training Visit and 13 weeks only)

3.2.2 Unscheduled Visits

Participants may have unscheduled visits during the study period if required for additional device training or other unanticipated needs per the study investigator discretion. Study participants will be instructed to upload their study device any time the participant changes device profile settings, and study staff will document review of these changes as an unscheduled visit. Documentation of the review must occur as an unscheduled visit if these changes are not being performed in window/part of the scheduled study visits and are not captured as part of a scheduled study visit.

3.2.3 Exercise and Meal Challenges

Participants will complete 3 meal and 3 exercise challenges during the study. Procedures are described in section 5.1.

3.3 Early Discontinuation of Study Device

Participants who discontinue the study device prior to 13 weeks, either by choice or by investigator decision, will be asked to come for an end of study visit and then will be dropped from the study. If the visit occurs at 6 weeks or after, blood will be drawn for the central laboratory HbA1c measurement.

Chapter 4: Study Devices and Drugs

4.1 Study Devices

The investigational device (CLC system) includes an insulin pump and a continuous glucose monitor.

4.1.1 Insulin Pump

The study system will include the Tandem t:slim X2 with Control-IQ 1.5 technology.

4.1.2 Continuous Glucose Monitoring

The study CGM that is part of the CLC system is the Dexcom G6, which includes a transmitter and sensors. The CGM sensor will be replaced at least once every 10 days.

4.1.3 Blood Glucose Meter

The study blood glucose meter is the Contour® NEXT (Ascencia Diabetes Care).

Blood glucose levels will be measured using the study's blood glucose meter (glucometer) and the CGM device will be calibrated if needed using the study glucometer and strips in accordance with the manufacturer's labeling.

4.1.4 Ketone Meter

The study blood ketone meter is the Precision Xtra Blood Glucose and Ketone Monitoring System (Abbott Diabetes Care).

Blood ketone levels will be measured when needed to evaluate prolonged hyperglycemia. The blood glucose meter component of the Precision Xtra device will not be used.

4.2 Study Device and Drug Accountability Procedures

Device accountability and inventory will be documented to include detailed inventory records of the study study CGM supplies, and Tandem insulin pump system.

4.3 Participant Access to Study Device at Study Closure

Participant will return all investigational study devices and supplies (insulin pump, CGM and related supplies) at study closure. Participant may keep the study ketone meter and study glucometer if these devices are not marked for investigational use only.

Chapter 5: Testing Procedures and Questionnaires

5.1 Meal and Exercise Challenges

Participants will complete 3 meal and 3 exercise challenges with the study device.

A minimum of 48 hours will occur between all challenges for each participant. Challenges may be performed in any order.

Participants will be instructed to communicate with study staff within one day prior to each challenge to review procedures and to have a contact with study staff after the completion of each challenge.

Hyperglycemia and Hypoglycemia treatment guidelines (sections 3.1.3 and 3.1.2) remain in effect for the challenges, and will be reviewed with participants prior to each challenge.

Participants will be reminded they must have a care partner, trained in these hypoglycemia and hyperglycemia treatment guidelines, present during the challenges and overnight until 6 AM the next day.

Site staff will directly contact the participant if they do not receive a follow up contact from participants when 24 hours have passed since the time of completion of the planned challenge.

5.1.1 Meal Challenges

The same meal should be used for each of the three meal challenges—either lunch or dinner (participant choice).

During study device use, the three meal challenges will consist of:

- No bolus for the meal
- 50% bolus - calculate the bolus dose using the bolus calculator, and deliver half the recommended dose of insulin.
- Full bolus for the meal based on calculated bolus dose using the bolus calculator.

For each meal challenge, participants will:

1. Be in a fasting state for two hours prior to consuming the meal and the last manual insulin bolus more than two hours prior to the meal.
2. Only begin the meal challenge if CGM glucose is between 70 mg/dL and 200 mg/dL. *Subjects with hyperglycemia > 200mg/dL will reschedule their challenge for another time. If < 70 mg/dL, carbohydrate treatment can be given, after which the meal challenge can continue.*
3. Consume at least 50 grams carbohydrate for the meal. *Each participant will use the same meal for all of their meal challenges in the study. Participants will be encouraged to use the same frozen entrée of their choice for consistency.*
4. Write down the start and end time of eating the meal, as well as the meal content (to include amount of carbohydrate, protein and fat) on the study provided logbook.
5. Not give an additional bolus for up to 3 hours after the meal challenge, unless BG is above 300 mg/dL for more than 1 hour, or symptoms of hyperglycemia develop.
6. Not take additional carbohydrates for up to 3 hours after the meal challenge, unless BG is < 70 mg/dL, or symptoms of hypoglycemia develop.
7. Not exercise for 3 hours after the meal challenge.
8. After the meal is completed, perform an SMBG (fingerstick) glucose check 1 hour after, prior to bed, and once overnight.

9. Notify the site within 24 hours after completion of each meal challenge.
10. The meal challenge will end 3 hours after the meal is completed.

5.1.2 Exercise Challenges

For each exercise challenge, participants will:

1. Have extra carbohydrate containing snacks and glucagon on hand during and after exercise.
2. Per their usual routine and investigator guidance, consider activation of "exercise activity" on the pump up to 45 minutes ahead of actual exercise, to allow for less insulin on board when starting exercise.
3. Consider reducing the last meal bolus prior to exercise as a way to reduce insulin on board and limit hypoglycemia.
4. Perform one hour of exercise, including at least half an hour of moderate activity. Exercise does not need to be the same activity each time.
5. Only begin exercise if CGM glucose is ≥ 120 mg/dL and CGM glucose is not trending downward.
6. Write down the start time of last meal and amount and time of last insulin dose, type of exercise performed, as well as the start and stop time of each exercise session in the study logbook *(as this may not correlate exactly with exercise activity use on the pump)*. Participants may take breaks if needed, as long as the full hour of activity is completed.
7. Stop the exercise challenges at any point for injury or development of new symptoms; development of chest pain/pressure, feeling unwell, development of hypoglycemic symptoms, undue shortness of breath, signs of poor perfusion (leg pain/claudication), or for any other reason.
8. After the exercise challenge is completed, perform an SMBG (fingerstick) glucose check 1 hour after, prior to bed, and once overnight.
9. Notify the site within 24 hours after completion of each exercise challenge. Participants will be asked if they developed new symptoms and review guidance on the need to stop future exercise challenges if any adverse events or new symptoms occurred per clinician judgement based on the severity of symptoms.
10. The exercise challenge will end after 1 hour of the required activity is completed.

5.2 Laboratory Testing

5.2.1 HbA1c

HbA1c measurement will be performed locally at the Screening visit.

An additional blood sample will be obtained (venipuncture or fingerstick) and sent to the central laboratory at the Control-IQ 1.5 Training visit and at the 13-week visit (or at early withdrawal of the subject from the study providing they have completed at least 6 weeks of follow-up).

5.2.2 Urine Pregnancy

Urine pregnancy testing performed locally at clinical site for females of child-bearing potential at the screening visit, at the start of study device use, and anytime pregnancy is suspected.

Chapter 6: Unanticipated Problem, Adverse Event, and Device Issue Reporting

6.1 Unanticipated Problems

Site investigators will promptly report to the Coordinating Center and Sponsor on an eCRF all unanticipated problems meeting the criteria below. For this protocol, an unanticipated problem is an incident, experience, or outcome that meets all of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied
- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research)
- Suggests that the research places participants or others at a greater risk of harm than was previously known or recognized (including physical, psychological, economic, or social harm)

The Coordinating Center will report to the IRB all unanticipated problems not directly involving a specific site such as unanticipated problems that occur at another participating entity such as a pharmacy or laboratory. These instances must be reported to the study IRB within seven calendar days of recognition. The Sponsor will report to the appropriate regulatory authorities if the IRB determines that the event indeed meets the criteria of an Unanticipated Problem requiring additional reporting.

6.2 Adverse Events

6.2.1 Definitions

Adverse Event (AE): Any untoward medical occurrence (including laboratory findings) associated with study procedures, the use of a device, biologic in a study participant, including any comparator used, irrespective of the relationship between the adverse event and the device(s) under investigation (referred to as *Adverse Reaction* when caused by a drug).

Serious Adverse Event (SAE): Any untoward medical occurrence that meets at least one of the following:

- 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 (sight 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).

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)).

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 (Note that an Adverse Event Form is to be completed in addition to a Device Issues Form, unless excluded from reporting as defined in section 6.2.2).

Comparator: Medical device, therapy (e.g. active treatment, normal clinical practice), placebo or no treatment, used in the control group in a clinical investigation. (ISO 14155:2020)

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 labeling for the device. The intended performance of a device refers to the intended use for which the device is labeled or marketed. (21 CFR 803.3). Note: for reporting purposes, sites will not be asked to distinguish between device complaints and malfunctions.

Use Error: User action or lack of user action while using the medical device (3.34) that leads to a different result than that intended by the manufacturer or expected by the user. Includes the inability of the user to complete a task. Use errors can result from a mismatch between the characteristics of the user, user interface, task or use environment. Users might be aware or unaware that a use error has occurred. An unexpected physiological response of the patient is not by itself considered a use error. A malfunction of a medical device that causes an unexpected result is not considered a use error. (ISO 14155:2020)

6.2.2 Reportable Adverse Events

A reportable adverse event includes all events meeting the definition of an adverse event, except for the following:

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

All reportable AEs—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 AE form online. Each AE form is reviewed by the Medical Monitor to assess safety and to verify the coding and the reporting that is required.

6.2.3 Hypoglycemic Events

Hypoglycemia is only reportable as an adverse event when one of the following criteria is met:

- a hypoglycemic event occurred meeting the following definition of severe hypoglycemia: the event required assistance of another person due to altered consciousness, and required another person to actively administer carbohydrate, glucagon, or other resuscitative actions. This means that the participant was 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 loss of consciousness. These episodes may be associated with sufficient neuroglycopenia to induce seizure or loss of consciousness. If glucose measurements are not available during such an event, neurological recovery attributable to the restoration of glucose to normal is considered sufficient evidence that the event was induced by a low glucose concentration.
- evaluation or treatment was obtained at a health care provider facility for an acute event involving hypoglycemia, or the participant contacted the site and received guidance following the occurrence of an acute event involving hypoglycemia

When a severe hypoglycemia event occurs (as defined above), an Adverse Event Form should be completed. Severe hypoglycemia events should be considered to be serious adverse events with respect to reporting requirements. When a severe hypoglycemia event occurs during use of a study device, it generally will be considered to be unrelated to the device (per section 6.2.5) if the device functioned as intended and there does not appear to be a flaw in how the device is intended to function.

6.2.4 Hyperglycemic/Ketotic Events

Hyperglycemia is only reportable as an adverse event when one of the following 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, or the participant contacted the site and received guidance on how to manage the hyperglycemia/ketosis
- blood ketone level ≥0.6 mmol/L, even if there was no communication with a health care provider at the time of the event

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 (or CO2) <15; and
- Treatment provided in a health care facility

When a hyperglycemia/ketotic event qualifies as an SAE as defined in section 6.2.1, an Adverse Event Form should be completed. Events meeting DKA criteria should be considered to be serious adverse events with respect to reporting requirements. Hyperglycemia events not meeting criteria for DKA

generally will not be considered as serious adverse events unless one of the SAE criteria in section 6.2.1 is met.

DKA can occur at "euglycemic" glucose levels less than 250 mg/dL, and may occur more commonly in individuals taking adjuvant medications for glucose control such as SGLT-2 inhibitors. This should be reported as a DKA event if it occurs.

When a hyperglycemia/DKA event occurs during use of a study device, it generally will be considered to be unrelated to the device (per section 6.2.5) if the device functioned as intended and there does not appear to be a flaw in how the device is intended to function.

6.2.5 Relationship of Adverse Event to Study Investigational Device

The study investigator will assess the relationship of any adverse event to the study device or study drug. The Medical Monitor also will make this assessment, which may or may not agree with that of the study investigator. Reporting requirements will be based on the Medical Monitor's assessment.

To ensure consistency of adverse event causality assessments, investigators should apply the following general guidelines when determining whether an adverse event is related to a study device or study drug:

Unrelated: The AE is clearly not related to a study drug/device and a likely alternative etiology exists such as an underlying disease, environmental or toxic factors or other therapy.

Unlikely Related: The AE does not follow a reasonable temporal sequence during or after use of study drug/device and a more likely alternative etiology exists such as an underlying disease, environmental or toxic factors, or other therapy.

Possibly Related: The AE occurred in a reasonable time during or after use of study drug/device; but could be related to another factor such as an underlying disease, environmental or toxic factors, or other therapy; and there is a possible, though weak, scientific basis for establishing a causal association between the AE and the study drug/device.

Probably Related: The AE occurred in a reasonable time during or after use of study drug/device; is unlikely to be related to another factor such as an underlying disease, environmental or toxic factors, or other therapy; and there is a plausible, though not strong, scientific basis for establishing a causal association between the AE and the study drug/device.

Definitely Related: The AE occurred in a reasonable time during or after use of study drug/device; cannot be explained by another factor such as an underlying disease, environmental or toxic factors, or therapy; and there is a strong scientific basis for establishing a causal association between the AE and the study drug/device.

Events determined to be *Possibly Related*, *Probably Related*, or *Definitely Related* will be considered 'Related' with respect to any required IRB and FDA reporting.

6.2.6 Severity (Intensity) of Adverse Events

The severity (intensity) of an adverse event will be rated on a three-point scale: (1) mild, (2) moderate, or (3) severe. A severity assessment is a clinical determination of the intensity of an event. 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, discomfort or concern to the participant and may interfere with daily activities, but is usually ameliorated by simple therapeutic measures and participant is able to continue in study.

SEVERE: Interrupts a participant's usual daily activities, causes severe discomfort, may cause discontinuation of study device, and generally requires systemic drug therapy or other treatment.

6.2.7 Expectedness

For a serious adverse event that is considered possibly related to study device, the Medical Monitor will classify the event as unexpected if the nature, severity, or frequency of the event is not consistent with the risk information previously described in the protocol, labeling, or Investigator Brochure.

6.2.8 Coding of Adverse Events

Adverse events will be coded using the MedDRA dictionary.

6.2.9 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).

If any reported adverse events are ongoing when a participant completes the study (or withdraws), adverse events classified as UADEs or related SAEs or SUSARs will be followed until they are either resolved, or have no prospect of improvement or change, even after the participant has completed all applicable study visits/contacts. For all other adverse events, data collection will end at the time the participant completes the study. Note: participants should continue to receive appropriate medical care for an adverse event after their participation in the study ends.

6.3 Reportable Device Issues

All UADEs and ADEs as defined in section 6.2.1 will be reported as both a 'device issues' and 'adverse event', except for skin reactions from CGM sensor placement or pump infusion set placement that do not require pharmacologic treatment.

Device complaints and device malfunctions will be reported except in the following circumstances. These occurrences are expected and will not be reported on a Device Issue Form assuming criteria for a UADE or ADE have not been met:

- CGM sensor lasting fewer days than expected per manufacturer
- CGM tape adherence issues
- Pump infusion set insertion lasting fewer days than expected per manufacturer
- Battery lifespan deficiency due to inadequate charging or extensive wireless communication
- Intermittent device component disconnections/communication failures not requiring system replacement or workaround/resolution not specified in user guide/manual.
- Device issues clearly addressed in the user guide manual that do not require additional troubleshooting

6.4 Timing of Event Reporting

SAEs possibly related to a study device, study drug, or study participation and UADEs must be reported by the site to the Sponsor within 1 working day of the site becoming aware of the event. This can occur via phone or email, or by completion of the appropriate eCRFs as applicable. If the form(s) are not initially completed, they should be competed as soon as possible after there is sufficient information to evaluate the event. All other reportable ADEs and other reportable AEs should be submitted by completion on the eCRF(s) within 7 days of the site becoming aware of the event.

The Sponsor will notify all participating investigators of any adverse event that is serious, related, and unexpected. Notification will be made within 10 working days after the Sponsor becomes aware of the event.

Each principal investigator is responsible for reporting serious study-related adverse events and abiding by any other reporting requirements specific to his/her Institutional Review Board or Ethics Committee.

Upon receipt of a qualifying event, the Sponsor will investigate the event to determine if a UADE has occurred, and if indicated, report the results of the investigation to all overseeing IRBs, and the FDA within 10 working days of the Sponsor becoming aware of the UADE per 21CFR 812.46(b). The Sponsor must determine if the UADE presents an unreasonable risk to participants. If so, the Sponsor 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 Sponsor makes this determination and no later than 15 working days after first receipt notice of the UADE.

The investigators are also required to report, without unjustified delay, all device complaints and malfunctions that could have led to a UADE, including device complaints and malfunctions, irrespective of whether an adverse event occurred.

6.5 Safety Oversight

The study Sponsor's Medical Director will serve as Medical Monitor, and will review all adverse events, including all cases of severe hypoglycemia and DKA, and adverse device events that are reported during the study. SAEs typically will be reviewed within 1 working day of reporting. Other AEs typically will be reviewed on a weekly basis, as per the study safety management plan.

The Medical Monitor will determine if the events require expedited reporting to FDA, IRB and/or all participating sites. In addition, the Medical Monitor will confirm the MedDRA code assigned and adjudicate events for relatedness to the study procedure and investigational device, assess seriousness and severity, and determine if the event the event is anticipated or unanticipated. Both the investigator's and

Medical Monitor's assessments will be recorded, however, the adjudication decision of the Medical Monitor will be used for the final classification of events, including relatedness to the study procedures and/or the investigational device, for the determination of safety endpoints and for all regulatory reports, product labeling, and publications or presentations.

6.6 Stopping Criteria

6.6.1 Participant Discontinuation of Study Device

In the case of an unanticipated system malfunction resulting in a severe hypoglycemia or DKA event (or a malfunction that could have led to severe hypoglycemia or DKA), use of the study device will be suspended for that participant while the problem is diagnosed. The UADE will be reported to the IRB and FDA. After assessment of the problem and any correction, use of the study device will not be restarted until approval is received from the IRB and FDA.

In the absence of a device malfunction, use of the study device by a participant will be discontinued if any of the following occur:

- The investigator believes it is unsafe for the participant to continue on the intervention. This could be due to the development of a new medical condition or worsening of an existing condition; or participant behavior contrary to the indications for use of the device that imposes on the participant's safety
- The participant requests that the treatment be stopped
- Participant pregnancy
- Two distinct episodes of DKA as defined in section 6.2.4
- Two distinct severe hypoglycemia events as defined in section 6.2.3
- One episode of DKA as defined in section 6.2.4 and one severe hypoglycemia event as defined in section 6.2.3

Each DKA or severe hypoglycemia event will be reviewed by the Medical Monitor with respect to determination of cause and whether the occurrence of the event can be attributed to use of the study device or study drug.

An additional requirement for continued study device use following a single DKA or severe hypoglycemia event will be that the site investigator believes that the event is unlikely to recur and that it is safe for the participant to continue to use the system. Additionally, if the Medical Monitor determines that the occurrence of the event indicates that it is not safe for the participant to continue to use the study device, use will be discontinued.

6.6.2 Criteria for Suspending or Stopping Overall Study

In addition to the suspension of device use due to a UADE as described in section 6.6.1, 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.

Closed-loop system use will also be suspended if there are three or more cases of severe hypoglycemia or three or more cases of hyperglycemia/ketotic events qualifying as SAEs across the entire study in participants who have initiated Control-IQ technology use. The IRBs and FDA will be notified. After assessment of the problem and any corrections are implemented, use of the closed-loop system may be restarted if approval is received from the IRBs and FDA.

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Chapter 7: Miscellaneous Considerations

7.1 Drugs Used as Part of the Protocol

Subjects may use their own Humalog (insulin lispro) or Novolog (insulin aspart) during the Treatment Period, however, Humalog or Novolog will be provided to the subject as part of the study.

7.2 Collection of Medical Conditions and Medications

Pre-Existing Conditions: Any medical condition that is either present at screening, a chronic disease, or a prior condition that could impact the participant's health during the course of the study (e.g., prior myocardial infarction or stroke) will be recorded.

Medical Conditions Developing During the Study: Medical conditions developing during the study will be reviewed by the investigator for their relationship to the study device.

Medications: All medications in use at the time of screening or added during the course of the study will be recorded. Nutraceuticals and preventative treatment also will be recorded. Medications only taken as needed either can be recorded when prescribed or only recorded if used during the study. Glucagon for treatment of severe hypoglycemia will only be recorded if used during the study.

7.3 Prohibited Medications, Devices, Treatments, and Procedures

Treatment with any insulin other than Humalog or Novolog insulin is not permitted with the study device.

Treatment with sulfonylureas, meglitinides or Symlin is not permitted.

No new additional non-insulin glucose lowering medications may be added during the trial.

Participants taking GLP-1 receptor agonists, DPP-4 inhibitors, and/or SGLT-2 inhibitors will be allowed to continue these medications if they are on a stable dose of such medication for the last 3 months. These participants will be instructed to perform additional glucose and ketone monitoring as specified in section 3.1.3 Training on Management of Hyperglycemia and 3.1.2 Training on Management of Hypoglycemia.

Medications used for weight loss will be allowed if the participant is on a stable dose of such medication for the last 3 months. No new medications for weight loss may be added during the trial.

Additional medications may be excluded per judgement of the investigator.

The investigational study devices (t:slim X2 insulin pump, Dexcom CGM sensor) 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 above.

7.4 Rescue Medications, Treatments, and Procedures

Each participant will be required to have a glucagon preparation for rescue therapy for severe hypoglycemia.

7.5 Pregnancy Reporting

If pregnancy occurs, the participant will be discontinued from the study. The occurrence of pregnancy will be reported to the Coordinating Center within seven days and to the IRB as an Unanticipated Problem within seven calendar days.

7.6 Participant Compensation

Participant compensation will be specified in the informed consent form.

7.7 Participant Withdrawal

Participation in the study is voluntary, and a participant may withdraw at any time. For participants who withdraw, their data will be used up until the time of withdrawal.

Chapter 8: Statistical Considerations

8.1 Statistical Hypotheses

The primary objective of the study is assessment of safety. Therefore, there is no formal statistical hypothesis testing for efficacy. Safety endpoints will be compared with historical published data.

8.2 Sample Size

The sample size of at least 30 completers of the trial was selected to have a reasonable number of hours of use, with each subject completing approximately 3 months use of the study system with the removal of the basal clipping feature, and not for assessing safety endpoints and is not based on statistical principles.

8.3 Outcome Measures

Primary Safety Endpoints

- Rate of severe hypoglycemia as defined in section 6.2.3
- Rate of diabetic ketoacidosis as defined in section 6.2.4
- Number of unanticipated adverse device effects
- Number of other serious adverse events

Secondary Safety Endpoints

- All reportable adverse events
- CGM hypoglycemia outcomes
    - Overall % time <54 mg/dL
    - Overall % time <70 mg/dL

Exploratory Endpoints

- Times in ranges-overall (70-180 mg/dL, >180 mg/dL, >250 mg/dL, 70-140 mg/dL)
- Mean glucose
- Overall variability (CV and SD)
- HbA1c change from baseline
- CGM metrics for hypoglycemia, hyperglycemia, and variability during daytime and nighttime

8.4 Analysis Datasets

Safety analysis set: All participants who initiate the Treatment Period and use the study device

CGM analysis set: Any member of the Safety Analysis Set who has at least 24 hours of CGM data during the Treatment Period. CGM data occurring within the meal and exercise challenge windows will not be included in this set.

Meal and exercise challenge set: Any member of the Safety Analysis Set who has at least 24 hours of CGM data during the Treatment Period. Only CGM data occurring within the meal and exercise challenge windows will be included in this set.

8.5 Statistical Methods

8.5.1 Analysis of the Safety Event Endpoints

Safety events (ie, not including CGM defined events) will be tabulated for each type of event as the number of events per participant, the number of participants with > 1 event, and the rate of events per 100 person-years.

Since study eligibility excluded participants with 2 or more severe hypoglycemia or DKA events in the prior 6 months, an unbiased comparison of the event rate during the Treatment Period with the pre-study event rate is not possible. Therefore, the severe hypoglycemia and DKA event rates will be compared with the T1D Exchange data,[4] which reported the frequency of 1 or more severe hypoglycemia and DKA events in the prior 3 months. The proportion of participants with events during the Treatment Period will be compared with the T1D Exchange frequency.

8.5.2 Analysis of CGM Endpoints

CGM metrics will be computed for the Treatment Period. CGM metrics will be computed over 24 hours, during daytime (6am-11:59pm), and during nighttime (12am-5:59am).

The main statistical comparison will be made between the Treatment Period and historical data.

8.5.3 Intervention Adherence

The following tabulations will be performed:

- Sensor use–percent time of use as a function of overall treatment period
- Closed loop system use–percent time of use as a function of overall treatment period
- % time in different operational modes as a function of overall treatment period

8.6 Protocol Adherence and Retention

The following tabulations and analyses will be performed to assess protocol adherence for the study:

- Number of protocol deviations
- Flow chart accounting for all enrolled participants
- Number of and reasons for unscheduled visits and phone calls
- Number of participants who were enrolled but did not enter the Treatment Period and reasons
- Number of participants who stopped treatment and reasons

8.7 Baseline Descriptive Statistics

Baseline demographic and clinical characteristics of the cohort of participants who initiate the Treatment Period will be summarized in a table using summary statistics appropriate to the distribution of each variable. Descriptive statistics will be displayed by treatment group for the following:

- Age
- Sex
- Race/Ethnicity
- Socio-economic factors (income, education, and/or insurance status)

- Diabetes duration
- HbA1c
- BMI
- Total daily insulin
- Prior severe hypoglycemia and DKA events

8.8 Additional Tabulations and Analyses

The following data will be tabulated at baseline and at or over 13 weeks

- Insulin metrics (units/kg): total daily insulin, total daily basal insulin, total daily bolus insulin (plus total daily manual bolus, total daily automated bolus)

8.9 Device Issues

The following tabulations will be performed with respect to device issues:

- Reported device issues according to type of issue

8.10 Planned Interim Analyses

No formal interim analyses are planned.

8.11 Subgroup Analyses

Results will be tabulated according to baseline HbA1c and total daily insulin.

8.12 Multiple Comparison/Multiplicity

Safety event endpoints will not be corrected for multiple comparisons.

8.13 Analysis of Meal and Exercise Challenges

The meal and exercise challenges will be analyzed with the same CGM metrics and safety outcomes above to be tabulated during and after (specifically to include the time period through 3 hours after each meal challenge [end of meal challenge] and through 2 hours after the completion of each exercise challenge) and overnight (12am-5:59am) after each challenge performed. Separate analysis will be conducted for each type of challenge. These challenge analysis periods will be excluded from the analysis of main CGM metrics.

Chapter 9: Data Collection and Monitoring

9.1 Case Report Forms and Other Data Collection

The main study data are collected on electronic case report forms (eCRFs). When data are directly collected in electronic case report forms, this will be considered the source data. For any data points for which the eCRF is not considered source (e.g. lab results that are transcribed from a printed report into the eCRF, data collected in the electronic medical record, study specific source worksheets, etc.), the original source documentation will be maintained in the participant's study chart or medical record. This source must be readily verifiable against the values entered into eCRF.

Electronic device data files are obtained from the study software and individual hardware components. These electronic device files are considered the primary source documentation.

HbA1c measurements will be performed locally for the screening visit, and by the central laboratory prior to closed-loop start and at end of study.

9.2 Study Records Retention

Each participating site will maintain appropriate medical and research records for this trial, in compliance with GCP and regulatory and institutional requirements for the protection of confidentiality of participants.

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.

9.3 Quality Assurance and Monitoring

Designated personnel from the Coordinating Center will be responsible for maintaining quality assurance (QA) and QC systems to ensure that the clinical portion of the trial is conducted and data are generated, documented and reported in compliance with the protocol, GCP and the applicable regulatory requirements, as well as to ensure that the rights and wellbeing of trial participants are protected and that the reported trial data are accurate, complete, and verifiable. Adverse events will be prioritized for monitoring.

A monitoring plan will be developed and revised as needed during the course of the study. Study conduct and monitoring will conform with 21 Code of Federal Regulations (CFR) 812. This plan will describe in detail who will conduct the monitoring, at what frequency monitoring will be done, at what level of detail monitoring will be performed, and the distribution of monitoring reports.

The data of most importance for monitoring at the site are participant eligibility and adverse events. Therefore, the monitoring plan will focus on these areas. As much as possible, remote monitoring will be performed in real-time with on-site monitoring performed to evaluate the verity and completeness of the key site data. Elements of the monitoring plan may include:

- Qualification assessment, training, and certification for sites and site personnel
- Oversight of Institutional Review Board (IRB) coverage and informed consent procedures
- Central (remote) data monitoring: validation of data entry, data edits/audit trail, protocol review of entered data and edits, statistical monitoring, study closeout
- On-site monitoring (site visits): source data verification, site visit report
- Agent/Device accountability
- Communications with site staff
- Patient retention and visit completion
- Quality control reports
- Management of noncompliance
- Documenting monitoring activities
- Adverse event reporting and monitoring

Coordinating Center representatives or their designees may visit the study facilities at any time in order to maintain current and personal knowledge of the study through review of the records, comparison with source documents, observation and discussion of the conduct and progress of the study. The investigational site will provide direct access to all trial related source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

9.4 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol, GCP, or procedure requirements. The noncompliance may be either on the part of the participant, the investigator, or the study site staff. A significant (or major) deviation is any deviation that departs from the established materials in such a way that it poses an increase in the risk to subjects, adversely affects the welfare, rights, or safety of the research subjects, or negatively influences the scientific study integrity. As a result of a significant deviation, a corrective and preventive action plan shall be developed by the site and implemented promptly.

The site PI/study staff is responsible for knowing and adhering to their IRB requirements. Further details about the handling of protocol deviations will be included in the monitoring plan.

Chapter 10: Ethics/Protection of Human Participants

10.1 Ethical 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.

10.2 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.

10.3 Informed Consent Process

10.3.1 Consent Procedures and Documentation

Informed consent is a process that is initiated prior to the individual's agreeing 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 to the participants and their families. Consent forms will be IRB-approved and the participant will be asked to read and review the document. The investigator 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. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing.

The participants should have the opportunity to discuss the study with their surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. The participants may withdraw consent at any time throughout the course of the trial. A copy of the informed consent document will be given to the participants 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.

10.3.2 Participant and Data Confidentiality

Participant confidentiality is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their agents. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

The study monitor, other authorized representatives of the sponsor, representatives of the IRB, regulatory agencies or 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) and pharmacy records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each 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 the reviewing IRB, institutional policies, sponsor requirements and applicable regulations.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored at the Coordinating Center. This will not include the participant's contact or identifying information, unless otherwise specified in the informed consent form. Rather, individual participants and their research data will be identified by a unique study identification number. The study data entry and study management systems used by clinical sites and by the Coordinating Center research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the Coordinating Center.

10.3.3 Future Use of Stored Specimens and Data

Data collected for this study will be analyzed and stored at the Coordinating Center. After the study is completed, a dataset will be provided to the study Sponsor.

No biologic specimens will be stored.

Chapter 11: References

1. Brown SA, Kovatchev BP, Raghinaru D, Lum JW, Buckingham BA, Kudva YC, Laffel LM, Levy CJ, Pinsker JE, Wadwa RP, Dassau E, Doyle FJ 3rd, Anderson SM, Church MM, Dadlani V, Ekhlaspour L, Forlenza GP, Isganaitis E, Lam DW, Kollman C, Beck RW; iDCL Trial Research Group. Six-month randomized, multicenter trial of closed-loop control in type 1 diabetes. N Engl J Med. 2019; 381:1707-1717.
2. Breton MD, Kanapka LG, Beck RW, Ekhlaspour L, Forlenza GP, Cengiz E, Schoelwer M, Ruedy KJ, Jost E, Carria L, Emory E, Hsu LJ, Oliveri M, Kollman CC, Dokken BB, Weinzimer SA, DeBoer MD, Buckingham BA, Cherñavvsky D, Wadwa RP; iDCL Trial Research Group. A randomized trial of closed-loop control in children with type 1 diabetes. N Engl J Med. 2020; 383:836-845.
3. Breton M, Kovatchev B. One year real-world use of the Control-IQ advanced hybrid closed loop technology. Diabetes Technol Ther. 2021;23:601-608.
4. Foster et al. State of type 1 diabetes management and outcomes from the T1D Exchange in 2016-2018. Diabetes Technol Ther. 2019; 21:66-72.