Adaptation of Insulin Delivery Settings to Improve Clinical Outcomes with AID Use

Study Sponsor:	Tandem Diabetes Care, Inc. 11075 Roselle Street San Diego, CA 92121
Study Number:	TP-0009348
Study Phase:	Feasibility
IDE Number:	G210262
Study Device:	1) t:slim X2 Insulin Pump with Control-IQ 1.0 technology 2) Settings initializer and adaptation algorithm
Protocol Chair:	Jordan Pinsker, MD
Date:	01 OCT 2021
Version:	2.0

Confidentiality Statement

12 **Protocol Revision History**

Version Number	Amendment Date	Brief Description of Changes
1.0	06 SEP 2021	Initial Version Submitted to FDA
2.0	01 OCT 2021	First Version Approved by FDA

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1 SITE PRINCIPAL INVESTIGATOR STATEMENT OF COMPLIANCE

Protocol Identifying Number:	TP-0009348
Protocol Name:	Adaptation of Insulin Delivery Settings to Improve Clinical Outcomes with AID Use
Protocol Version / Date:	2.0 / 01 OCT 2021

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

The undersigned confirms that the trial will be conducted and documented in accordance with the US Federal, State and Local requirements for a post-market human clinical study, the protocol, and the stipulations of the clinical trial agreement.

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): _____

2 TERMS, ACRONYMS, ABBREVIATIONS

Abbreviation	Definition
ADE	Adverse Device Effect
AE	Adverse Event
CGM	Continuous Glucose Monitoring
CRF	Case Report Form
Control-IQ System	t:slim X2 insulin pump with Control-IQ technology
DKA	Diabetic Ketoacidosis
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HbA1c	Hemoglobin A1c
HCL	Hybrid Closed-loop
ICF	Informed Consent Form
QC	Quality Control
SAE	Serious Adverse Event
t:connect	t:connect diabetes management system
T1D	Type 1 diabetes
TDD	Total Daily Dose
UADE	Unanticipated Adverse Device Effect

3 PROTOCOL SYNOPSIS

Protocol Title	Initialization and Adaptation of Insulin Delivery Settings to Improve Clinical Outcomes with AID Use
Device	1) t:slim X2 insulin pump with Control-IQ technology (Control-IQ System) 2) An automatic settings initializer and adaptation system running on the server
Type of Study	Prospective, Single Arm, Single Center Feasibility Study
Rational	The purpose of this study is to obtain preliminary safety and performance data on a settings initialization and adaptation algorithm used in conjunction with closed-loop control. Based on data from simulations and current system use, an algorithm to more accurately initialize settings and adapt them over time, faster than typical HCP visits, would benefit users onboarding from multiple daily injections (MDI) and help them reach optimal glycemic outcomes faster. Outcomes of this study will allow for the determination of an optimal product configuration for adaptive settings and the ability to clinically test a commercial version of the new product for effectiveness.
Objectives	**Primary objective:** To demonstrate the safety of the system, by assessing the number of severe hypoglycemic events (needing assistance) compared to expected incidence **Secondary objective**: Compare time in range metrics and adverse events in the full 24 hour period, overnight and during the day, after each week of settings adaptation. The number of physician overrides/physician initiated changes in pump settings will also be tracked.
Primary Endpoints	1) Primary Endpoint: a. To demonstrate the safety of the system, by assessing the number of severe hypoglycemic events (needing assistance) compared to expected incidence 2) Secondary Endpoints: a. Time in range 70-180 mg/dL b. Time < 54 mg/dL c. Time < 70 mg/dL d. Time > 180 mg/dL e. Time > 250 mg/dL f. Time in tight glycemic range 70-140 mg/dL g. Post-prandial glycemic peak h. 4-hour post meal glucose AUC i. Sensor glucose median and interquartile range j. CGM metrics daytime vs. nighttime k. CGM metrics compared each week after adaptation l. DKA

	m. Adverse Device Effects n. Serious Adverse Events o. Change in total daily insulin use, basal and bolus p. Number of physician overrides/physician initiated changes in pump settings q. Patient Reported Outcomes
Duration of Study	Up to 17 weeks total, to allow for 2 to 4 weeks of CGM run-in if needed, then 13 weeks of pump/AID use with weekly settings adaptation
Study Design	Adults (age ≥ 18 years of age) with type 1 diabetes, who are using multiple daily injections, will be required to collect baseline CGM data for the first 2 weeks if not already Dexcom G6 users with at least 11 of 14 days of CGM use for the 14 days prior to enrollment. They may repeat this 14 day run-in period if adequate CGM data is not collected, or study staff feel it is necessary to continue to monitor their insulin dose. Subjects will then proceed to pump/Control-IQ training, where an algorithm performed on a paper worksheet will be used to recommend initial basal rate, carbohydrate ratio and correction factor settings. Subjects will then wear the insulin pump with Control-IQ technology active for 13 weeks, and at day 3 and at the end of each week will: 1) Upload their pump using the USB uploader 2) Have their study physician review the settings recommendations on the pump download report that will appear after each download. 3) Change their settings after being called by the study physician to match the new recommendations. 4) Upload their pump again so the study physician can verify the settings have been changed appropriately, and verify the correct settings have been applied to the correct pump assigned to the subject by verifying the serial number on the recommendations report to the changes in t:connect. 5) Physicians can at any time adjust pump settings and override the settings adaptation recommendations for safety concerns, and convert scheduled phone follow-up visits to in clinic visit at their discretion. A semi-structured one-on-one interview may be completed concurrent with the 13-Week Visit or within a 28-day period following that visit. The interview will last approximately 30 minutes and will be conducted by Tandem staff using a script of open-ended questions to gather feedback and reactions to the

	automated initialization and adaptation system, as well as the use of Closed-Loop Control.
Study Population	Male and female subjects ≥ 18 years of age with type 1 diabetes, who are current MDI users, who have a baseline A1c at screening between 7.5 to 11%
Number of Subjects	Up to 45 subjects may sign the consent form and be screened, with the goal that 30 subjects start use of the study device, and at least 20 subjects complete the trial.
Number of Sites	1 clinical site in the United States
Main Criteria for Inclusion	Eligibility to enroll in the study will be assessed based on the following inclusion criteria: 1. Adult subjects ≥ age 18 years 2. Clinical diagnosis of type 1 diabetes for at least one year 3. Using a basal/bolus regimen by injection (MDI therapy) 4. Total daily dose ≥10 units/day 5. Willing to use only aspart (novolog) or lispro (humalog) U-100 insulin with the study pump. 6. A1c ≥ 7.5% and ≤ 11% at screening 7. Not pregnant or planning a pregnancy during the time period of the study. 8. Has current glucagon product to treat severe hypoglycemia (injectable or nasal) at home (will provide prescription if they do not have one) 9. Willingness to follow study procedures and a signed informed consent form
Main Criteria for Exclusion	Eligibility to enroll in the study will be assessed based on the following exclusion criteria: 1. Two or more episodes of severe hypoglycemia (needing assistance) in the past 6 months 2. Two or more episodes of diabetic ketoacidosis 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. Significant chronic kidney disease or hemodialysis 6. Significant liver disease 7. History of adrenal insufficiency 8. History of abnormal TSH consistent with hypothyroidism or hyperthyroidism that is not appropriately treated 9. Other chronic disease/condition determined by investigator to interfere with participation in the study 10. Use of glucocorticoids, beta blockers or other medications determined by investigator to interfere with study

	11. Use of long-acting insulin, inhaled insulin (Afrezza), or use of any non-insulin glucose lowering agents (i.e. SGLT-2 inhibitor) other than Metformin with the study pump 12. Subject is pregnant or lactating or intending to become pregnant before or during participation in this study. 13. Investigator judgement that subject would not be able to complete the trial.
Procedures in Screening/Baseline Period	At screening, baseline data will be collected. For Decom G6 users, mean/median sensor glucose, TIR and all glycemic outcomes will be recorded as baseline data if data is available for the at least 11 of the last 14 days. Those without adequate baseline data will collect Dexcom G6 sensor data to establish a baseline over the next 2 weeks.
Management of Adverse Events	Safety information will be collected weekly during study clinic phone calls, or more frequently if a severe AE occurs. The event, date of onset, severity, seriousness, duration and relationship to the device/adaptation system will be documented. All reported device-related AEs will be followed until they are adequately resolved or stabilized, or until study completion/termination, whichever comes first.
Statistical Analysis	Descriptive statistics will be used to evaluate rates of AEs as well as glycemic outcomes over time as the algorithm adapts insulin delivery settings.

The study will be conducted and documented in accordance with the IRB, FDA, ICH and GCP guidelines.

4 BACKGROUND

4.1 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 A_{1c} (HbA_{1c}) level of 7.0% for children and adults. These findings indicate the need for better approaches to type 1 diabetes management.

Recent estimates suggest that approximately 400,000 U.S. patients with type 1 diabetes (T1D) use insulin pumps. Adoption of pump therapy varies by geography and may be related to healthcare provider preference or patient characteristics and socioeconomic status. Use of insulin pumps is more common in individuals of higher socioeconomic status as reflected by race/ethnicity, private health insurance, family income, and education. Additionally, referrals from healthcare providers and insurance approvals are critical determinants for who becomes a pump user in the United States.

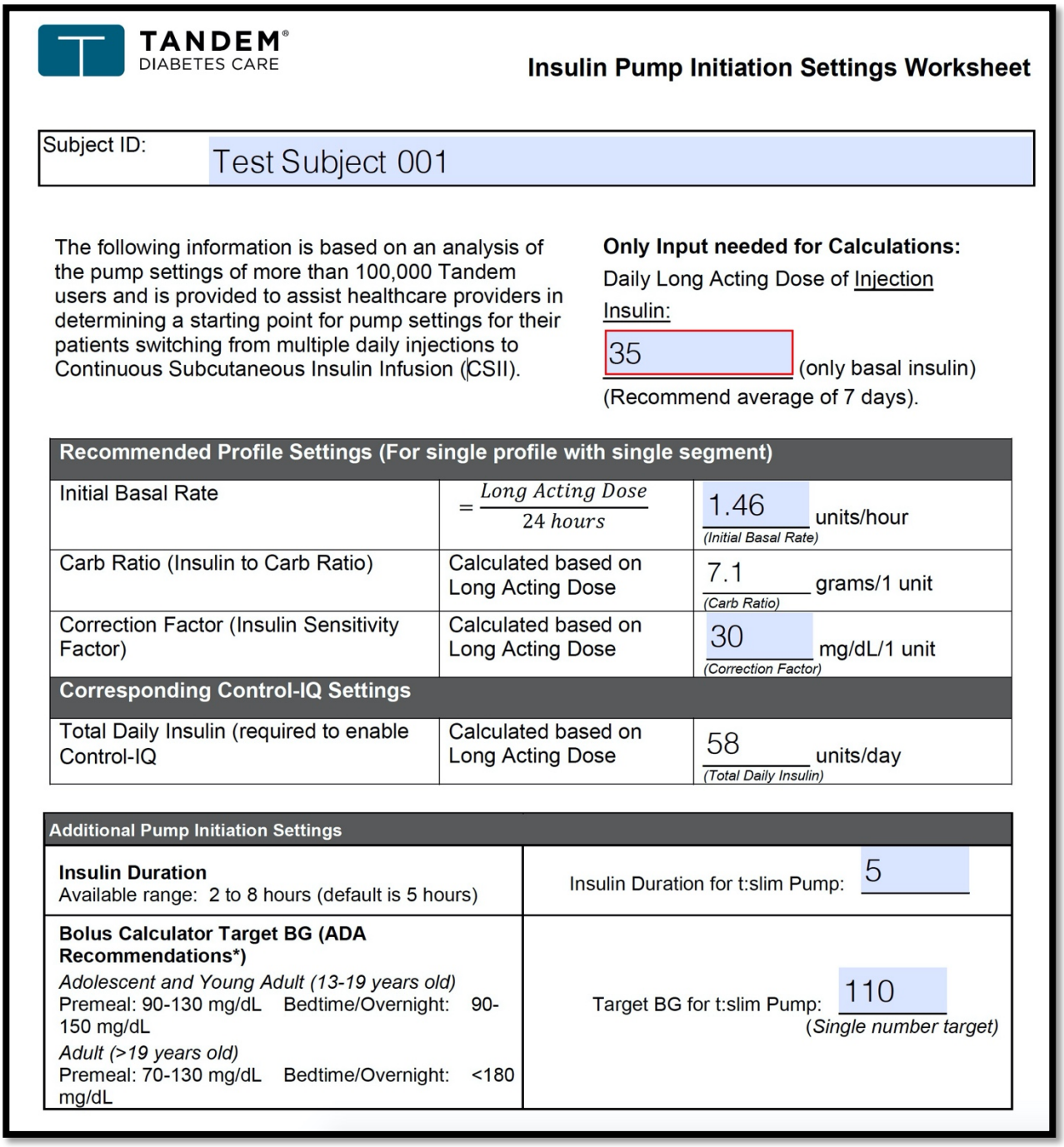
However, a main barrier to starting pump therapy and staying on it is having to enter insulin delivery settings into the pump (ie basal rate, carbohydrate ratio, correction factor) and optimizing those settings for each individual. In this trial, we will test the safety and feasibility of using a settings initializer for individuals onboarding to the t:slim X2 pump with Control-IQ technology, with weekly adaptations of insulin delivery settings over ~13 weeks.

4.2 DEVICE BACKGROUND

The t:slim X2 insulin pump with Control-IQ technology is an advanced hybrid closed-loop (HCL) system, developed and manufactured by Tandem Diabetes Care, Inc. and cleared in the U.S. by the FDA for individuals with type 1 diabetes. Control-IQ is integrated with the Dexcom G6 continuous glucose monitor (CGM) and uses CGM values to predict glucose values 30 minutes in the future. Based on the predicted glucose, Control-IQ modulates basal insulin delivery, and delivers automated correction boluses to mitigate impending hyperglycemia. The current Control-IQ system is FDA approved down to age 6 years old for individuals with type 1 diabetes, and has been found to improve time in range (70-180 mg/dL) and decrease both time < 70 mg/dL and time >180 mg/dL (1,2).

4.3 SETTINGS OPTIMIZER

For this study, insulin delivery settings initialization will use a paper worksheet (Figure 1) to guide initial settings.



TANDEM DIABETES CARE

Insulin Pump Initiation Settings Worksheet

Subject ID: Test Subject 001

The following information is based on an analysis of the pump settings of more than 100,000 Tandem users and is provided to assist healthcare providers in determining a starting point for pump settings for their patients switching from multiple daily injections to Continuous Subcutaneous Insulin Infusion (CSII).

Only Input needed for Calculations:
Daily Long Acting Dose of Injection Insulin:
35 (only basal insulin)
(Recommend average of 7 days).

Recommended Profile Settings (For single profile with single segment)		
Initial Basal Rate	$= \frac{Long\ Acting\ Dose}{24\ hours}$	1.46 units/hour (Initial Basal Rate)
Carb Ratio (Insulin to Carb Ratio)	Calculated based on Long Acting Dose	7.1 grams/1 unit (Carb Ratio)
Correction Factor (Insulin Sensitivity Factor)	Calculated based on Long Acting Dose	30 mg/dL/1 unit (Correction Factor)
Corresponding Control-IQ Settings		
Total Daily Insulin (required to enable Control-IQ	Calculated based on Long Acting Dose	58 units/day (Total Daily Insulin)

Additional Pump Initiation Settings	
Insulin Duration Available range: 2 to 8 hours (default is 5 hours)	Insulin Duration for t:slim Pump: 5
Bolus Calculator Target BG (ADA Recommendations*) *Adolescent and Young Adult (13-19 years old)* Premeal: 90-130 mg/dL Bedtime/Overnight: 90-150 mg/dL *Adult (>19 years old)* Premeal: 70-130 mg/dL Bedtime/Overnight: <180 mg/dL	Target BG for t:slim Pump: 110 (*Single number target*)

Figure 1. Insulin pump initiation settings worksheet

Adaptation will be recommended by the automated system, emailing written recommendations for settings changes to physicians for their review. The automated settings adaptation system will recommend a single basal rate, carbohydrate ratio and correction factor throughout the day (Figure 2), and will limit recommendations to a maximum 5% change at a time.

```
Report for serial number 660396 generated at 2021-07-14 08:02

Data was analyzed from  2021-06-12 08:00:00 to 2021-06-18 15:54:45 (last
upload date)

Recommendations are based on the most frequently used profile (Main)

           Current  Recommended
    BR      2.500     2.500
    CR       4.0       4.0
   ISF        19        19

There were no settings changes during this period

The profile 'Main' used the following segment(s):
   Time       BR        CR       ISF
 12:00 AM    2.5       4.0        19


Recommended settings aim to limit the amount of time below a specific
glucose level if no changes to settings are made
Estimated probability of going below 70 mg/dL during basal:      0.46%
Estimated probability of going below 110 mg/dL during basal:      6.15%
Estimated probability of going below 70 mg/dL postprandially:      0.50%
Estimated probability of going below 110 mg/dL postprandially:     10.22%

Number of times we estimate hypoglycemic treatments were
given in response to predicted lows during basal:        0
Number of times we estimate hypoglycemic treatments were
given in response to predicted lows postprandially: 1
```

Figure 2. Sample E-Mailed Adaptation Settings Recommendations

If the user or study staff has manually changed settings to more than one timepoint per day, the settings adaptation system will continue to adapt back to one setting per day for basal rate, carbohydrate ratio and correction factor as shown in Figure 3.

Report for serial number 91634002 generated at 2021-07-14 07:59

Data was analyzed from 2020-08-29 12:59:19 to 2020-09-04 23:59:43. There was no upload during this period

Recommendations are based on the most frequently used profile (Weekday)

	Current	Recommended
BR	0.250	0.237
CR	30	28
ISF	135	128

Settings were changed at the following time(s):

Profile Name	
Weekday	2020-08-29 12:55:00
Weekday	2020-08-29 12:55:38
Weekday	2020-08-29 12:56:13
Weekday	2020-08-29 12:56:43
Weekday	2020-08-29 12:57:14
Weekday	2020-08-29 12:58:15
Weekday	2020-08-29 12:59:00
Weekday	2020-08-29 12:59:19
Weekend	2020-08-29 13:05:09
Weekend	2020-08-29 13:07:57
Weekend	2020-08-29 13:10:06
Weekend	2020-08-29 13:10:46
Weekend	2020-08-29 13:13:41
Weekend	2020-08-29 13:14:17
Weekend	2020-08-29 13:14:43
Weekend	2020-08-29 13:14:59

The profile 'Weekday' used the following segment(s):

Time	BR	CR	ISF
12:00 AM	0.38	30.0	135
02:00 AM	0.25	12.0	130
06:00 AM	0.28	10.0	120
08:00 AM	0.28	13.0	120
12:00 PM	0.34	20.0	95
02:00 PM	0.44	13.0	90
06:00 PM	0.44	18.0	85
09:00 PM	0.4	18.0	85

Figure 3. Sample E-Mailed Adaptation Settings Recommendations where more than one time point was entered, and the system has changed back to one time point to continue adaptation. The report notes all the dates and times settings were changed since the last report.

Physician overrides of the system, or changes to pump settings between emailed recommendations, will be documented with the reason for the override/settings change on the study case report form.

5 STUDY OBJECTIVES, DESIGNS AND ENDPOINTS

5.1 STUDY OBJECTIVES

Primary objective: To demonstrate the safety of the settings initialization and adaptation algorithm when in conjunction with Control-IQ technology, by assessing the number of severe hypoglycemic events (needing assistance) compared to expected incidence

Secondary objective: Compare time in range metrics and adverse events in the full 24 hour period, overnight and during the day, after each week of settings adaptation. The number of physician overrides/physician initiated changes in pump settings will also be tracked.

5.2 STUDY DESIGN

This feasibility study is a prospective, single arm study, evaluating an algorithm to recommend insulin pump settings at pump start (initialization) and then adjust settings at 3 days, at 7 days, and then weekly through 13 weeks.

Adults (age ≥ 18 years of age) with type 1 diabetes, who are using multiple daily injections, will be required to collect baseline CGM data for the first 2 weeks if not already Dexcom G6 users with at least 11 of 14 days of CGM use for the 14 days prior to enrollment. They may repeat this 14 day run-in period if adequate CGM data is not collected, or study staff feel it is necessary to continue to monitor their insulin dose.

Up to 45 subjects may sign the consent form and be screened, with the goal that up to 30 subjects start use of the study device, and at least 20 subjects complete the trial.

Enrollment goals for baseline A1c at screening are:

- At least 5 subjects with A1c 8% - 8.9%
- At least 5 subjects with A1c ≥ 9%

Subjects will then proceed to pump/Control-IQ training, where an algorithm based worksheet will be used to recommend initial basal rate, carbohydrate ratio and correction factor settings.

Subjects will then wear the insulin pump with Control-IQ technology active, and at 3 days after training, 7 days after training, and then every 7 days will:

1) Upload their pump using the USB uploader
2) Have their study physician review the settings recommendations on the pump download report that will appear after each download.
3) Change their settings after being called by the study physician to match the new recommendations.
4) Upload their pump again so the study physician can verify the settings have been changed appropriately, and the correct settings changes were implemented on the correctly assigned pump by looking at the pump serial number on the settings report.

Physicians can at any time adjust pump settings and override the settings adaptation recommendations for safety concerns, and convert scheduled phone follow-up visits to in clinic visit at their discretion.

After 13 weeks (3 months) of use, subjects will return to clinic for a final visit.

Subjects who agree to provide their contact information will be offered an open ended interview at the end of the study to discuss their confidence in the automated settings recommendations and how it worked for them.

The data collected in this study will be directly entered into the eCRF (as applicable) or paper source forms. Subject data will include demographics, focused medical history, therapy data, and baseline and follow-up measures. All device data will be collected digitally and downloaded directly into the manufacturer provided software for the study devices.

5.3 STUDY ENDPOINTS

1) Primary Endpoint:
    a. To demonstrate the safety of the system, by assessing the number of severe hypoglycemic events (needing assistance) compared to expected incidence
2) Secondary Endpoints:
    a. Time in range 70-180 mg/dL
    b. Time < 54 mg/dL
    c. Time < 70 mg/dL
    d. Time > 180 mg/dL
    e. Time > 250 mg/dL
    f. Time in tight glycemic range 70-140 mg/dL
    g. Post-prandial glycemic peak
    h. 4-hour post meal glucose AUC
    i. Sensor glucose median and interquartile range
    j. CGM metrics daytime vs. nighttime
    k. CGM metrics compared each week after adaptation
    l. DKA
    m. Serious Adverse Events
    n. Adverse Device Effects
    o. Change in total daily insulin use, basal and bolus
    p. Number of physician overrides/physician initiated changes in pump settings
    q. Patient Reported Outcomes

6 SUBJECT SELECTION

6.1 SUBJECT POPULATION

6.1.1 INCLUSION CRITERIA:

Eligibility to enroll in the study will be assessed based on the following inclusion criteria:

1) Adult subjects ≥ age 18 years
2) Clinical diagnosis of type 1 diabetes for at least one year
3) Using a basal/bolus regimen by injection (MDI therapy)
4) Total daily dose ≥10 units/day
5) Willing to use only aspart (novolog) or lispro (humalog) U-100 insulin with the study pump.
6) A1c ≥ 7.5% and ≤ 11% at screening
7) Not pregnant or planning a pregnancy during the time period of the study.
8) Has current glucagon product to treat severe hypoglycemia (injectable or nasal) at home (will provide prescription if they do not have one)
9) Willingness to follow study procedures and a signed informed consent form

6.1.2 EXCLUSION CRITERIA:

Eligibility to enroll in the study will be assessed based on the following exclusion criteria:

1) Two or more episodes of severe hypoglycemia (needing assistance) in the past 6 months
2) Two or more episodes of diabetic ketoacidosis 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) Significant chronic kidney disease or hemodialysis
6) Significant liver disease
7) History of adrenal insufficiency
8) Hypothyroidism or hyperthyroidism that is not appropriately treated
9) Other chronic disease/condition determined by investigator to interfere with participation in the study
10) Use of glucocorticoids, beta blockers or other medications determined by investigator to interfere with study
11) Use of long-acting insulin, inhaled insulin (Afrezza), or use of any non-insulin glucose lowering agents (i.e. SGLT-2 inhibitor) other than Metformin with the study pump
12) Subject is pregnant or lactating or intending to become pregnant before or during participation in this study.
13) Investigator judgement that subject would not be able to complete the trial.

6.2 SUBJECT WITHDRAWAL OR TERMINATION

Subjects are free to withdraw from the study at any time and will be withdrawn if they inform the study team that they no longer wish to participate. Data collected prior to the subject's withdrawal will remain part of the study record and will be included in the analyses.

7 TREATMENT OF SUBJECTS

7.1 THE T:SLIM X2 INSULIN PUMP WITH CONTROL-IQ TECHNOLOGY

The Control-IQ System is a US FDA approved device indicated for the treatment of type 1 diabetes in people age 6 years and older. The Control-IQ System is integrated with the Dexcom G6 CGM and uses CGM values to adjust insulin delivery with the goal of improving glucose control (time in range of 70-180 mg/dL).

For the current study, subjects will use t:slim X2 pump with Control-IQ technology cleared under K201214 and K200467, respectively.

7.2 ENROLLMENT PROCEDURE:

Potential study subjects will be recruited by the clinical site. After a description of the study is provided by the study team, the subject will be asked to sign the informed consent form (ICF). Eligibility to enroll in the study will be assessed based on the inclusion/exclusion criteria. Enrollment information will be entered onto the study case report forms. In addition, demographic and relevant medical history will be collected at this time and entered onto the study case report forms.

7.3 DURATION OF THERAPY AND FOLLOW-UP:

Each enrolled subject may participate for ~17 weeks total, to allow for 2 to 4 weeks of CGM run-in if needed, then 13 weeks of pump/AID use with weekly settings adaptation.

7.4 STUDY PROCEDURES:

Event Schedule: The CRFs will be completed by the investigator (or an authorized member of the investigator's staff) per the event schedule described below.

Table 1. Schedule of Visits and Procedures

	Screening Visit	CGM Run-in Visit (may be repeated after 2 weeks)	Pump and Control-IQ Training Visit	Control-IQ Use					
		2-4 weeks		3d	7d	Weekly	13w	F/U Call	UV
Visit (V) or Contact (C)	V	V	V	C	C	C	V	C	C/V
Informed Consent	X								
Eligibility Assessment	X								
Medical history/ physical exam	X								
Vital Signs	X								
HbAlc (POC or local lab for inclusion criteria confirmation)	X								
HbA1c (Central lab)			X				X		
Pregnancy test (females of child-bearing potential)	X		X						
Assessment of CGM use	X	X							
Study system training		X	X						
AE Assessment		X	X	X	X	X	X	X	X
Upload device data from home				X	X	X			X
Download device data at clinic visit	X	X	X				X		X
Open Ended Interview							X		

Baseline Data Collection: Adults (age ≥ 18 years of age) with type 1 diabetes, who are using multiple daily injections, will be required to collect baseline CGM data for the first 2 weeks if not already Dexcom G6 users with at least 11 of 14 days of CGM use for the 14 days prior to enrollment. They may repeat this 14 day run-in period if adequate CGM data is not collected.

Subject Completion or Early Withdrawal: The subject completes the study approximately 17-21 weeks after enrollment, or when they choose to withdraw from the study, if earlier than the final visit

Data Collection: Investigators will assign a de-identified number to each subject and will be required to keep any study paperwork or electronic files in a secure private area. Monitoring will be conducted to help ensure that data is secure and entered within reasonable limits, consistent with a risk-based monitoring approach.

Demographics: The following demographic data will be obtained: date of birth, gender, race, ethnicity, educational level, socioeconomic status, residence, employment status, weight, height, blood pressure, pulse, and type of health insurance.

Medical History: Medical history, including existing comorbidities deemed clinically relevant (e.g. retinopathy, nephropathy, neuropathy, history of cardiovascular events) will be collected at baseline. In addition, details specific to type 1 diabetes, including age at diagnosis, duration of disease, and previous therapy will be collected from the study subject and documented in the subject's eCRF. A new hemoglobin A1c will also be obtained at the screening visit, at randomization and at end of study.

Pregnancy: In order to reduce the risk of pregnancy, subjects of childbearing potential must agree to use an effective method of birth control while participating in this study. Acceptable methods of birth control for use in this study are barrier methods, intrauterine devices, or oral contraceptive pills. The Investigator or study staff will discuss this with the subject.

Device Training: All subjects will complete study device training before starting use of the study device. Subjects will be trained by qualified study staff using the study approved device training checklists, and will be given a copy of the Study Participant Instruction Sheet. In addition to device training, the Study Participant Instruction Sheet reviews procedures for checking ketones, and when to contact study staff for assistance.

All subjects will complete CGM training. Subjects who are not already Dexcom G6 users with at least 11 of 14 days of CGM use for the 14 days prior to enrollment will complete CGM run-in. They may repeat this 14 day run-in period if adequate CGM data is not collected.

All subjects will complete insulin pump training. The pump training visit may be extended over more than one day if needed in the judgement of the investigator. Initial pump settings will be configured by following the study settings algorithm worksheet. At the end of the pump training visit, subjects will activate Control-IQ technology

Subjects will wear the insulin pump with Control-IQ technology active in the outpatient setting, and have scheduled phone follow up visits at 3 days (+/- 1 day), 7 days (+/- 2 days), then weekly (+/- 3 days). A final visit in clinic will occur at 13 weeks (+/- 7 days). A post final clinic visit phone call will occur 3 days (+/- 1 day) after changing back to MDI therapy after the study devices are returned.

At each visit, the study pump and CGM data will be downloaded, and insulin delivery settings as recommend by the algorithm will be emailed to study staff for provider review. Providers will call the subjects for their scheduled appointment, and have the subjects enter the new pump settings, and then re-upload their pump to confirm the changes were implemented correctly, verifying the settings were applied to the correct pump serial number as assigned to that subject.

At any time, study staff providers may override the algorithm settings recommendations, either at or in between scheduled visits for safety concerns. The reason for any changes to override pump settings will be documented.

Unscheduled visits may occur at any time, and may be initiated by stuff stay or by study subjects.

A semi-structured one-on-one interview may be completed concurrent with the 13-Week Visit or within a 28-day period following that visit. The interview will last approximately 30 minutes and will be conducted by Tandem staff using a script of open-ended questions to gather feedback and reactions to the automated initialization and adaptation system, as well as the use of Closed-Loop Control.

Interview sessions may be audio- or video-taped and transcribed by a professional transcription service. Otherwise, these recordings will not be shared for any non-study purposes. Transcriptions will use a code for participants, such as "Participant 1", and will not contain names or other identifiers of participants.

Observation and Recording of Adverse Events: Subjects will be required to report AEs. Open-ended questions and questions specific to SH and DKA will be included in all subject visits. An AE form will be completed for every adverse event reported by a subject. Any medical management of an event and the resolution of the event must be recorded in source documentation and on the appropriate eCRF using medical terminology.

Treatment of hyper- and hypoglycemia: Procedures in Section 10.9 and 10.10 will be followed by study staff and by subjects.

7.5 EARLY TERMINATION VISIT (IF APPLICABLE)

Participants will be asked to come for an end of study visit in the event of withdrawal or early termination.

7.6 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 staff may adjust insulin delivery settings on the study pump at any time, and override the algorithm recommendations for safety concerns, and will document these changes.

7.7 FINAL CLINIC VISIT

Subjects will return all study supplies and complete the study surveys.

A final central lab HbA1c will be drawn.

All study devices (glucose meter, ketone meter, insulin pump and CGM) will be downloaded.

Participants will be permitted to keep the blood glucometer, blood ketone meter and any remaining CGM sensors at the end of the study, but will need to return all other devices, including insulin pump and related supplies.

Subjects will complete the Diabetes Impact and Device Satisfaction (DIDS) Scale, and be asked to provide their contact information for a final interview phone call.

Study staff will then supervise the participants transition back to their standard of care therapy.

- 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.

- Doses will be adjusted to best match the current daily insulin requirements from CSII use, typically = (total daily dose + 20%)/2, with further modification as per clinical site usual practice.

- Study staff will confirm subjects have carbohydrates on hand for their drive back home, and instruct subjects to check their glucose levels when they arrive at home, prior to bedtime, and at least one time overnight on the first night to monitor for hypoglycemia, reminding subjects that insulin on board can be active for the next few hours even after stopping their pump.

7.8 POST STUDY PHONE CALL

All participants will have a post-study phone call 3 (±1) days after the date of their final visit and transition back to their prior insulin therapy, during which the following will occur:

- Check on transition back to usual home diabetes care

- Assessment of adverse events

8 STATISTICAL CONSIDERATIONS

8.1 STATISTICAL ANALYSIS:

This feasibility study is a prospective, single arm study, evaluating al algorithm to recommend insulin pump settings at pump start (initialization) and then weekly for 13 weeks.

Descriptive statistics of the rates of severe hypoglycemia, DKA, and serious adverse events will be reported for baseline (with CGM run-in data) and compared to changes after each weekly adaptation. Additionally, descriptive statistics of glycemic outcomes will for baseline and each intervention configuration will be provided.

The statistics will include all primary and secondary outcomes of the study as listed in section 5.3. These statistics will be calculated at the patient-level, and a sub-analysis of daytime vs. nighttime statistics will be provided.

9 RISKS AND BENEFITS

9.1 POTENTIAL RISKS AND BENEFITS OF THE DEVICE

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

9.2 VENIPUNCTURE RISKS

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

9.3 FINGERSTICK RISKS

About 1 drop of blood will be removed by fingerstick for measuring blood glucose and sometimes Hemoglobin A1c (HbA1c) or other tests. This is a standard method used to obtain blood for routine hospital laboratory tests. Pain is common at the time of lancing. In about 1 in 10 cases, a small amount of bleeding under the skin will produce a bruise. A small scar may persist for several weeks. The risk of local infection is less than 1 in 1000. This should not be a significant contributor to risks in this study as fingersticks are part of the usual care for people with diabetes.

9.4 SUBCUTANEOUS CATHETER RISKS (CGM)

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

On rare occasions, the CGM may break and leave a small portion of the sensor probe under the skin that may cause redness, swelling or pain at the insertion site. The participant will be instructed to notify the study coordinator immediately if this occurs.

9.5 RISK OF HYPOGLYCEMIA

As with any person having diabetes and using insulin, there is always a risk of having a low blood sugar (hypoglycemia). The frequency of hypoglycemia should be no more and possibly less than it would be as part of daily living. Symptoms of hypoglycemia can include sweating, jitteriness, and not feeling well. Just as at home, there is the possibility of fainting or seizures (convulsions) and that for a few days the participant may not be as aware of symptoms of hypoglycemia. A CGM functioning poorly and significantly over-reading glucose values could lead to inappropriate insulin delivery.

9.6 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. All subjects will be issued a glucose meter and glucose test strips, and a ketone meter and ketone strips to use to carefully monitor for hyperglycemia and be given instructions on how to mitigate hyperglycemia should it occur.

9.7 RISK OF DEVICE REUSE

All devices will be used by a single study participant only. There will be no device re-use.

9.8 OTHER RISKS

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

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

Data downloaded from the CGM, pump, and the home glucose and ketone meter will be collected for the study as measures of diabetes self-management behaviors. The downloaded data from the subject's home pump will include data from prior to the date of the screening visit. Some people may be uncomfortable with the researchers' having such detailed information about their daily diabetes habits.

9.9 KNOWN POTENTIAL BENEFITS

Participants may experience a significant improvement in glucose control. Hypoglycemia is the number one fear of many individuals taking insulin and this fear often prevents optimal glycemic control. Hyperglycemia will likely be reduced as well.

It is expected that this protocol will yield increased knowledge about using an automated closed-loop to control glucose levels in people with type 1 diabetes. The individual participant may or may not benefit from study participation.

9.10 RISK ASSESSMENT

Based on the facts that (1) adults and adolescents with type 1 diabetes experience mild hypoglycemia and hyperglycemia frequently as a consequence of the disease and its management, (2) the study intervention involves periodic automated insulin dosing that may

increase the likelihood of hypoglycemia, and periodic automated attenuation of insulin delivery that may increase the likelihood of hyperglycemia, (3) mitigations are in place, and have been tested in prior studies using the investigational device system in the home setting, that limit the likelihood of excessive insulin dosing or prolonged withdrawal of insulin, (4) rapid reversal of hypoglycemia and hyperglycemia can be achieved, and (5) the Control algorithm (Control-IQ) is already FDA approved for and has shown significant (10+%) TIR improvements in individuals with type 1 diabetes, it is the assessment of the investigators that this protocol falls under DHHS 46.405 which is a minor increase over minimal risk. In addition, it is the belief of the investigators that this study also presents prospect of direct benefit to the participants and general benefit to others with diabetes.

9.11 GENERAL CONSIDERATIONS

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

10 DESCRIPTION OF THE STUDY DEVICES AND USE

All study supplies will be provided by Tandem Diabetes Care, Inc.

10.1 INSULIN PUMP

The study system will include the Tandem t:slim X2 insulin pump with Control-IQ technology cleared under K201214 and K200467 respectively (Tandem Diabetes Care, San Diego, CA).

10.2 CONTINUOUS GLUCOSE MONITORING

The study CGM will include Dexcom G6 transmitter and sensors. The CGM sensor will be replaced at least once every 10 days or as per manufacturer instructions.

10.3 BLOOD GLUCOSE METER AND STRIPS

Blood glucose levels will be measured using the study-assigned 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. (Contour NEXT or Contour NEXT ONE, Ascensia Diabetes Care US, Inc., 5 Wood Hollow Rd, Parsippany, NJ 07054 USA)

10.4 KETONE METER AND STRIPS

Blood ketone levels will be measured using the Abbott Precision Xtra meter and strips in accordance with the manufacturer's labeling. The blood glucose meter component of the Precision Xtra device will not be used. (Abbott Diabetes Care Inc., 1360 South Loop Road, Alameda, CA 94502 USA)

10.5 STUDY DEVICE ACCOUNTABILITY PROCEDURES

Device accountability and inventory will be documented in each subject's study chart, to include detailed inventory records of the study glucose meter, study ketone meter, study CGM supplies, and Tandem insulin pump system.

10.6 BLOOD GLUCOSE METER TESTING

- QC testing will be performed before issuing the blood glucose meter to a subject. Additional QC testing may be performed per manufacturer guidelines.
- A tested meter will not be used in a study if it does not read within the target range concentration per manufacturer labeling.
- Participants will be reminded to use the study blood glucose meter for all fingerstick blood glucose measurements.
- Participants will be asked to perform fingerstick blood glucose measurements in accordance with the labelling of the study CGM device.

10.7 BLOOD KETONE TESTING

- QC testing will be performed before issuing the blood ketone meter to a subject. Additional QC testing may be performed per manufacturer guidelines.
- A tested meter will not be used in a study if it does not read within the target range concentration per manufacturer labeling.
- Participants will be instructed on how to perform blood ketone testing.
- Participants will be given guidelines for treatment of elevated blood ketones.

10.8 CGM CALIBRATION

Throughout the study, participants will be instructed to calibrate the study CGM in accordance with manufacturer labelling.

10.9 HYPERGLYCEMIA SAFETY PROTOCOL

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.

10.10 HYPOGLYCEMIA SAFETY PROTOCOL

When using the study device, hypoglycemia low threshold alerts will be set to no lower than 70 mg/dL, and if a participant's CGM reading is <70 mg/dL, subjects will be instructed to treat with ~15 grams of carbohydrate, and perform fingerstick testing as necessary per CGM manufacturer instructions.

11 ADVERSE EVENTS, DEVICE ISSUES, AND STOPPING RULES

11.1 ADVERSE EVENTS

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

Serious Adverse Event (SAE): Any untoward medical occurrence that:

Results in death.

Is life-threatening; (a non-life-threatening event which, had it been more severe, might have become life-threatening, is not necessarily considered a serious adverse event).

Requires inpatient hospitalization or prolongation of existing hospitalization.

Results in persistent or significant disability/incapacity or substantial disruption of the ability to conduct normal life functions (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 Deficiency or Issue Form).

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.

11.2 REPORTABLE ADVERSE EVENTS

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

1. A serious adverse event
2. An Adverse Device Effect as defined in section 11.1, unless excluded from reporting in section 11.9
3. An Adverse Event occurring in association with a study procedure
4. Hypoglycemia meeting the definition of severe hypoglycemia as defined below
5. Diabetic ketoacidosis (DKA) as defined below or in the absence of DKA, a hyperglycemic or ketosis event meeting the criteria defined below

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

Pregnancy occurring during the study will be recorded.

11.3 HYPOGLYCEMIC EVENTS

Hypoglycemia not associated with an Adverse Device Effect is only reportable as an adverse event when the following definition for severe hypoglycemia is met: the event required assistance of another person due to altered consciousness, and required another person to actively administer carbohydrate, glucagon, or other resuscitative actions. 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 coma. These episodes may be associated with sufficient neuroglycopenia to induce seizure or coma. If plasma glucose measurements are not available during such an event, neurological recovery attributable to the restoration of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration.

11.4 HYPERGLYCEMIC EVENTS/DIABETIC KETOACIDOSIS

Hyperglycemia not associated with an Adverse Device Effect is only reportable as an adverse event when one of the following 4 criteria is met:

the event involved DKA, as defined by the Diabetes Control and Complications Trial (DCCT) and described below

evaluation or treatment was obtained at a health care provider facility for an acute event involving hyperglycemia or ketosis

blood ketone level ≥0.6 mmol/L and communication occurred with a health care provider at the time of the event

- blood ketone level ≥2.5 mmol/L, even if there was no communication with a health care provider

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

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

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

11.5 RELATIONSHIP OF ADVERSE EVENT TO STUDY DEVICE

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

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

Yes

There is a plausible temporal relationship between the onset of the adverse event and the study intervention, and the adverse event cannot be readily explained by the participant's clinical state, intercurrent illness, or concomitant therapies; and/or the adverse event follows a known pattern of response to the study intervention; and/or the adverse event abates or resolves upon discontinuation of the study intervention or dose reduction and, if applicable, reappears upon re-challenge.

No

Evidence exists that the adverse event has an etiology other than the study intervention (e.g., preexisting medical condition, underlying disease, intercurrent illness, or concomitant medication); and/or the adverse event has no plausible temporal relationship to study intervention.

11.6 INTENSITY OF ADVERSE EVENT

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

MILD: Usually transient, requires no special treatment, and does not interfere with the participant's daily activities.

MODERATE: Usually causes a low level of inconvenience or concern to the participant and may interfere with daily activities, but is usually ameliorated by simple therapeutic measures.

SEVERE: Interrupts a participant's usual daily activities and generally requires systemic drug therapy or other treatment.

11.7 CODING OF ADVERSE EVENTS

Adverse events will be coded using the MedDRA dictionary. The investigator's assessment will be recorded.

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

11.8 OUTCOME OF ADVERSE EVENT

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

RECOVERED/RESOLVED – The participant recovered from the AE/SAE without sequelae. Record the AE/SAE stop date.

RECOVERED/RESOLVED WITH SEQUELAE – The event persisted and had stabilized without change in the event anticipated. Record the AE/SAE stop date.

FATAL – A fatal outcome is defined as the SAE that resulted in death. Only the event that was the cause of death should be reported as fatal. AEs/SAEs that were ongoing at the time of death; however, were not the cause of death, will be recorded as "resolved" at the time of death.

NOT RECOVERED/NOT RESOLVED (ONGOING) – An ongoing AE/SAE is defined as the event was ongoing with an undetermined outcome.

An ongoing outcome will require follow-up by the site in order to determine the final outcome of the AE/SAE.

The outcome of an ongoing event at the time of death that was not the cause of death, will be updated and recorded as "resolved" with the date of death recorded as the stop date.

UNKNOWN – An unknown outcome is defined as an inability to access the participant or the participant's records to determine the outcome (for example, a participant that was lost to follow-up).

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

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

11.9 REPORTABLE DEVICE ISSUES

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

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

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

11.10 PREGNANCY REPORTING

If pregnancy occurs, the participant will be discontinued from the study. The occurrence of pregnancy will be reported on an AE Form.

11.11 TIMING OF EVENT REPORTING

SAEs and UADEs must be recorded within 24 hours via completion of the serious adverse event form and sponsor notification.

Other reportable adverse events, device malfunctions (with or without an adverse event), and device complaints should be reported promptly by completion of the relevant case report form, but there is no formal required reporting period.

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

Upon receipt of a UADE report, the study principal investigators will investigate the UADE and if indicated, report the results of the investigation to the sites' IRBs, and the Sponsor (Tandem Diabetes Care) within ten working days of becoming aware of the UADE per 21CFR 812.46(b)

(2). The Sponsor must determine if the UADE presents an unreasonable risk to participants. If so, all investigations, or parts of investigations presenting that risk, will be 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.

In the case of a device system component malfunction (e.g. pump, CGM, control algorithm), information will be forwarded to the responsible company by the site personnel, to be handled by its complaint management system.

11.12 PARTICIPANT DISCONTINUATION OF STUDY DEVICE

Rules for discontinuing study device use are described below.

1) 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*
2) The participant requests that the treatment be stopped
3) Participant pregnancy
   If pregnancy occurs, the participant will be discontinued from the study entirely. Otherwise, even if the study device system is discontinued, the participant will be encouraged to remain in the study through the final study visit.
4) Two distinct episodes of DKA as defined in section 11.4
5) Two distinct episodes of severe hypoglycemia as defined in section 11.3
6) The investigator may have a subject temporarily stop use of Control-IQ during: periods of significant illness, temperature >101.5, use of oral or injectable glucocorticoids, use of epinephrine for the emergency treatment of a severe allergic reaction or asthma attack, or if a subject is going to the hospital for any reason. If the investigator believes the period if illness may be prolonged or put the safety of the subject or the overall study at risk, the investigator may withdraw the subject from the study.

11.13 CRITERIA FOR SUSPENDING OR STOPPING OVERALL STUDY

1) In the case of a system malfunction resulting in a severe hypoglycemia or severe hyperglycemia event (as defined in sections 11.3 and 11.4), use of the study device system will be suspended while the problem is diagnosed.

2) Three or more cases of severe hypoglycemia or three or more cases of severe hyperglycemia (as defined in sections 11.3 and 11.4) across the entire study.

3) In addition, study activities could be similarly suspended if the manufacturer of any constituent study device requires stoppage of device use for safety reasons (e.g. product recall). The affected study activities may resume if the underlying problem can be corrected by a protocol or system modification that will not invalidate the results obtained prior to suspension.

The Sponsor (Tandem Diabetes Care) will be informed of all serious adverse events and any unanticipated adverse device events that occur during the study and will review compiled safety data at periodic intervals. The Sponsor will request suspension of study activities or stoppage of the study if deemed necessary based on the totality of safety data available.

11.14 SAFETY OVERSIGHT

The clinical site principal investigator will review all reported adverse events and adverse device effects, and report them to the study sponsor.

As this is a single site clinical feasibility study, the Medical Director from the study sponsor will carefully review all adverse event reports, and adjudicate their relationship the study device based on the site principal investigator's report and all available information.

12 MISCELLANEOUS CONSIDERATIONS

12.1 DRUGS USED AS PART OF THE PROTOCOL

Participants will use either lispro or aspart insulin prescribed by their personal physician. Participants not using lispro or aspart insulin at the time of screening may not start use of the study device until they have one of these insulins available to them for use.

12.2 PROHIBITED MEDICATIONS, TREATMENTS, AND PROCEDURES

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

Treatment with any non-insulin glucose-lowering agent other than metformin (including GLP-1 agonists, Symlin, DPP-4 inhibitors, SGLT-2 inhibitors, sulfonylureas and naturaceuticals) or Afrezza will not be permitted during the trial.

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

12.3 PARTICIPANT COMPENSATION

Participant compensation will be specified in the informed consent form.

12.1 PARTICIPANT ACCESS TO STUDY DEVICE AT STUDY CLOSURE

Participant will return all 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.

13 DATA COLLECTION AND MONITORING

13.1 CASE REPORT FORMS AND DEVICE DATA

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

When data are directly collected in electronically, this will be considered the source data. The clinical site will maintain appropriate medical and research records for this trial, in compliance with ICH E6 and regulatory and institutional requirements for the protection of confidentiality of participants.

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

13.2 STUDY RECORDS RETENTION

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

13.3 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. As a result of deviations, corrective actions are to be developed by the site and implemented promptly. The site PI/study staff is responsible for knowing and adhering to their IRB reporting requirements.

13.4 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.

13.5 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.

13.6 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.

13.7 PARTICIPANT AND DATA CONFIDENTIALITY

The study monitor, other authorized representatives of the sponsor, such as the study coordinating center, representatives of the IRB or authorized representatives from the clinical site(s) or Tandem Diabetes Care, Inc., may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records (office, clinic, or hospital) for the participants in this study. The clinical study sites 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 local IRB and Institutional regulations.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted from the clinical site(s) and sent to Tandem Diabetes Care. This will not include the participant's contact or identifying information. 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 the clinical site will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the clinical site(s). Permission to transmit data will be included in the informed consent.

Subject information will be managed according to the Health Insurance Portability and Accountability Act of 1996 (HIPAA). In addition, all personal data will be handled in accordance with the EU directive e95/46/EC and as of 25 May 2018 in accordance with the GDPR. All data will be de-identified at each site before being entered into the case report forms.

Only the investigator and site coordinator will have access to the de-identified data. The Informed Consent Form must include information letting the subject know:

- What protected health information (PHI) will be collected during the study;
- Who will have access to that information;
- Who will use or disclose that information;
- The rights of the research subject to revoke their authorization for use of their PHI.

13.8 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.

13.9 CONFIDENTIALITY

For security and confidentiality purposes, participants will be assigned an identifier that will be used instead of their name. Protected health information gathered for this study will be securely stored at the clinical site. De-identified participant information may also be provided to the Sponsor consistent with these guidelines.

14 REFERENCES

1. Brown SA, Kovatchev BP, Raghinaru D, Lum JW et al. Six-month randomized, multicenter trial of closed-loop control in type 1 diabetes. *N Engl J Med*. 2019; 381(18):1707-1717.
2. Breton MD, Kanapka LG, Beck RW, Ekhlaspour L et al. A randomized trial of closed-loop control in children with type 1 diabetes. *N Engl J Med*. 2020; 383(9):836-845.