Medtronic

Study Title	Evaluation of Meal Gesture Dosing in Adults with Type 1 Diabetes
NCT Number	NCT04964128
Document Description	Clinical Investigational Plan (Version F)
Document Date	31-MAR-2022

Medtronic

Clinical Investigation Plan

Clinical Investigation Plan/Study Title	Evaluation of Meal Gesture Dosing in Adults with Type 1 Diabetes
Clinical Investigation Plan Identifier	339
Study Product Name	**Investigational Products:** ▪ MiniMed™ 780G insulin pump, with investigational software version 1.0W.1003 – referred to as the study pump throughout this protocol ▪ Guardian™ Link 3 transmitter ▪ Klue™ Health App by Klue, Inc. with investigational software release tag 1.0 ▪ Klue™ Health App by Klue, Inc. with investigational software release tag 2.0, once available ▪ Roche Accu-Chek™ Guide Link Glucose Meter with modification to allow communication with study pump – referred to as the study meter throughout this protocol **Non-Investigational Products:** ▪ Guardian™ Sensor 3 – referred to as the sensor throughout this protocol ▪ CareLink™ System (for clinical research) – referred to as CareLink system throughout this protocol ▪ CareLink™ Personal (for clinical research) – referred to as CareLink Personal throughout this protocol ▪ FoodPrint™ app by Nutrino™ ▪ MiniMed Clinical app, with software version 1.1.1 ▪ CareLink Clinical app, with software version 2.1.1 ▪ FreeStyle Optium Neo or other locally approved meter to be used for blood ketone measurements only - referred to as the ketone meter throughout this protocol ▪ Roche Accu-Chek™ Guide Link Glucose Meter or other compatible commercially available Roche glucose meter – referred to as the study meter throughout this protocol **Other Commercially Available Products:** ▪ Apple Watch® ▪ Apple iPhone® **Other Products:** ▪ [redacted] once available

	▪ [redacted] once available
Sponsor/Local Sponsor	Medtronic MiniMed, Inc. (Global Sponsor) ("Medtronic") 18000 Devonshire St Northridge, CA 91325 Medtronic International Trading Sàrl (Local) ("Medtronic") Route du Molliau 31 1131 Tolochenaz, Switzerland
Document Version	F
Version Date	31-MAR-2022
Document Reference Number	D00456959

1. Investigator Agreement and Signature Page

Study product Name	**Investigational Product** ▪ MiniMed™ 780G insulin pump, with investigational software version 1.0W.1003 - referred to as the study pump throughout this protocol ▪ Guardian™ Link 3 transmitter ▪ Klue™ Health App by Klue, Inc., with investigational software release tag 1.0 ▪ Klue™ Health App by Klue, Inc., with investigational software release tag 2.0, once available ▪ Roche Accu-Chek™ Guide Link Glucose Meter with modification to allow communication with study pump – referred to as the study meter throughout this protocol **Non-Investigational Product** ▪ Guardian™ Sensor 3 - referred to as the sensor throughout this protocol ▪ CareLink™ System (for clinical research) – referred to as CareLink system throughout this protocol ▪ CareLink™ Personal software (for clinical research) – referred to as CareLink Personal throughout this protocol ▪ FoodPrint™ app by Nutrino™ ▪ MiniMed Clinical app, with software version 1.1.1 ▪ CareLink Clinical app, with software version 1.1.2 ▪ FreeStyle Optium Neo or other locally approved meter to be used for blood ketone measurements only - referred to as ketone meter throughout this protocol ▪ Roche Accu-Chek™ Guide Link Glucose Meter or other compatible commercially available Roche glucose meter – referred to as the study meter throughout this protocol **Other Commercially Available Products:** ▪ Apple Watch® ▪ Apple iPhone® **Other Products:** ▪ [redacted], once available ▪ [redacted], once available
Sponsor	Medtronic International Trading Sàrl (“Medtronic”) Route du Molliau 31 1131 Tolochenaz, Switzerland

Clinical Investigation Plan Identifier	**CIP339**
Version Number/Date	**Version F / Date 31-MAR-2022**

I have read the protocol, including all appendices, and I agree that it contains all necessary details for me and my staff to conduct this study as described. I will conduct this study as outlined herein and will make a reasonable effort to complete the study within the time designated.

I agree to comply with International Standard ISO 14155:2020 (Clinical investigation of medical devices for human subjects — Good clinical practice), the Israeli MOH Guidelines for Clinical Trials in Human Subjects, the protocol, and the applicable regulatory authority requirements. I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation and conduct of the clinical investigation without the prior written consent of Medtronic.

I will provide all study personnel under my supervision copies of the protocol and access to all information provided by Medtronic. I will discuss this material with them to ensure that they are fully informed about the products and the study.

Investigator's Signature:	
Investigator's Name:	
Institution:	
Date:	

Table of Contents

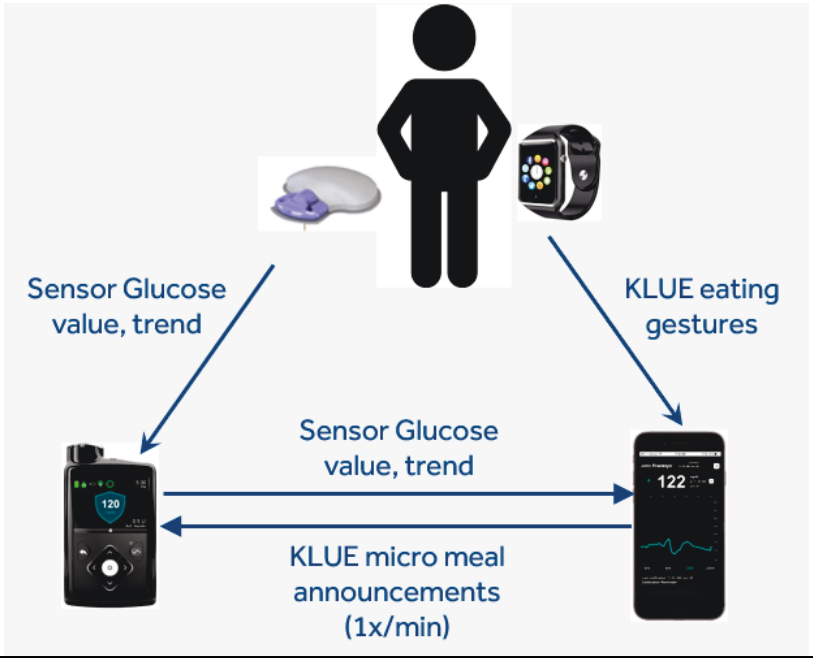
2. Glossary

Abbreviation	Definition
ADE	Adverse Device Effect
AE	Adverse Event
AHCL	Advanced Hybrid Closed Loop
ASIC	Application Specific Integrated Circuit (ASIC)
AUC	Area Under Curve
BG	Blood Glucose
CEC	Clinical Event Committee
CIP	Clinical Investigation Plan
CGM	Continuous Glucose Monitoring
CRO	Clinical Research Organization
CRF	Case Report Form
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DD	Device Deficiency
DKA	Diabetic Ketoacidosis
DoH	Declaration of Helsinki
eCRF	Electronic Case Report Form
EIS	Electrochemical Impedance Spectroscopy
EMEA	Europe Middle East Africa
EOS	End of Study
ER	Emergency Room
EC/HREB/Ethics Board	Ethics Committee
FD	Financial Disclosure
GCP	Good Clinical Practice
IB	Investigator Brochure
ICF	Informed Consent Form
ICH	International Conference of Harmonization
IFU	Instructions For Use
ISO	International Organization for Standardization
MOH	Ministry of Health
OC-RDC	Oracle Clinical Remote Data Capture
QC	Quality Control
RA	Regulatory Authority
RF	Radio Frequency
RT-CGM	Real-Time Continuous Glucose Monitoring
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SG	Sensor Glucose
SID	Subject Identification
SMBG	Self-Monitoring of Blood Glucose
TDD	Total Daily Dose

Abbreviation	Definition
USADE	Unanticipated Serious Adverse Device Effect

3. Synopsis

Title	Evaluation of Meal Gesture Dosing in Adults with Type 1 Diabetes
Clinical Study Type	Feasibility; Evaluation of meal gesture dosing within the Advanced Hybrid Closed Loop (AHCL) System in adults with type 1 diabetes
Study Product Name & Product Status	**Investigational/Non-CE-Marked Products Provided During Study:** ▪ MiniMed™ 780G insulin pump, with investigational software version 1.0W.1003 – referred to as the study pump throughout this protocol ▪ Guardian™ Link 3 transmitter ▪ Klue™ Health App by Klue, Inc. with investigational software release tag 1.0 ▪ Klue™ Health App by Klue, Inc. with investigational software release tag 2.0, once available ▪ Roche Accu-Chek™ Guide Link Glucose Meter with modification to allow communication with study pump – referred to as the study meter throughout this protocol **Non-Investigational/CE-Marked Product Provided During Study:** ▪ Guardian™ Sensor 3 – referred to as sensor throughout this protocol ▪ CareLink™ system (for clinical research) -– referred to as CareLink system throughout this protocol ▪ CareLink™ Personal (for clinical research) software – referred to as CareLink Personal throughout this protocol ▪ FoodPrint™ app by Nutrino™ ▪ MiniMed Clinical app, with software version 1.1.1 ▪ CareLink Clinical app, with software version 1.1.2 ▪ FreeStyle Optium Neo or other locally approved meter to be used for blood ketone measurements only – referred to as ketone meter throughout this protocol ▪ Roche Accu-Chek™ Guide Link Glucose Meter or other compatible commercially available Roche glucose meter – referred to as the study meter throughout this protocol **Other Commercially Available Products:** ▪ Apple Watch® ▪ Apple iPhone® **Other Products:** ▪ [redacted], once available ▪ [redacted] once available Consumables and accessories will be provided during the study (detailed list in **Appendix 18.5**).
Global Sponsor (Funding Source)	Medtronic MiniMed, Inc. ("Medtronic")

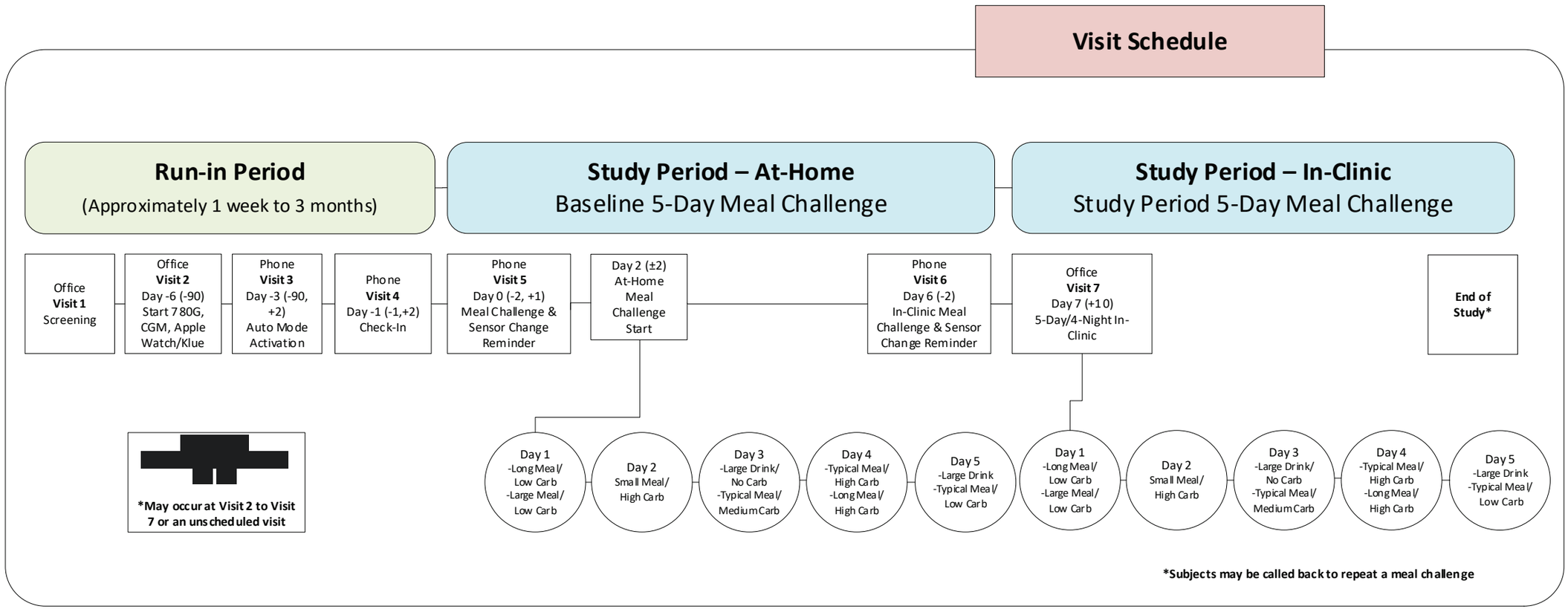
	18000 Devonshire St Northridge, CA 91325 866.948.6633
Local Sponsor	Medtronic International Trading Sàrl. ("Medtronic") Route du Molliau 31 1131 Tolochenaz, Switzerland
Indication under investigation	Type 1 diabetes
Purpose	The purpose of this study is to evaluate subject safety of using the Klue Health app utilizing meal gesture micro insulin dosing (meal gesture dosing) within the AHCL system in adult subjects with type 1 diabetes in a clinic setting.
Objective(s)	The objective of the study is to collect data for meal gesture dosing for unannounced meals within the AHCL System to be used for development of Medtronic Diabetes devices and products.
Study Design	This study is a single-center, single arm study in adult subjects with type 1 diabetes utilizing AHCL System with meal gesture detection and micro dosing (meal gesture dosing). Meal gesture dosing is a mode whereby meal announcements are not entered manually by the user. Instead, when meal gesture dosing is active, meal announcements are generated automatically by the system based on the detection of eating gestures and micro doses of insulin are given. See **Figure 1** for an overview. **Figure 1. AHCL System with Meal Gesture Dosing** 

	Overall subject participation will be approximately 3 weeks to 6 months. ▪ A total of up to 40 subjects (aged 18-75) may be enrolled at one investigational center in Israel to have at least 16 subjects complete the study. Subjects may repeat participation in the study at the request of the Sponsor and at the discretion of the investigator but will only be counted once toward the total number of subjects. The study consists of a run-in period and a study period. The run-in period is intended to allow subjects to become familiar with using the study pump system with the SmartGuard feature active and wearing the watch. Subjects should use the same insulin they will be using during the study period. Subjects will also be using the [redacted] with [redacted] During the first week of the study period, subjects will undergo a 5-day at-home baseline meal challenge at specific meal(s) on each day. The Klue app will be set to monitoring-mode. After run-in period and completion of the 5-day at-home study period with baseline meal challenges, study subjects will check into the clinic for a 5-day (4 nights) intervention. Study subjects will wear the system with Klue meal gesture dosing activated for the entire duration of the 5-day intervention. See **Section 10** for more details.
Sample Size and Investigational Site	A total of up to 40 subjects will be enrolled at one investigational center in Israel to have at least 16 subjects complete the study. Subjects may repeat participation in the study at the request of the Sponsor and at the discretion of the investigator will only be counted once toward the total number of subjects.
Duration	The study is anticipated to last approximately 15 months from investigational center initiation to finalization of all data entry and monitoring procedures. Subject participation is expected to be approximately 3 weeks to 6 months.
Inclusion Criteria	**General Inclusion Criteria:** 1. Is age 18-75 years at time of screening 2. Has a clinical diagnosis of type 1 diabetes for 2 years or more as determined via source documentation 3. Pump therapy for greater than 6 months prior to screening 4. Real-time continuous glucose monitoring (RT-CGM) experience greater than 3 months prior to screening 5. Must have a minimum daily insulin requirement (Total Daily Dose) of greater than or equal to 8 units 6. Is willing to perform ≥2 fingerstick blood glucose measurements daily 7. Is willing to perform required sensor calibrations 8. Is willing to wear the system continuously throughout the study

	9. If subject has celiac disease, it has been adequately treated as determined by the investigator 10. If the subject has had any of the following cardiovascular events more than 1 year prior to of screening: myocardial infarction, unstable angina, coronary artery bypass surgery, coronary artery stenting, transient ischemic attack, cerebrovascular accident, angina, congestive heart failure, or ventricular rhythm disturbances they should be cleared by a cardiologist prior to participation, if deemed necessary by the investigator. 11. If the subject has had any of the following cardiovascular events within 1 year of screening: myocardial infarction, unstable angina, coronary artery bypass surgery, coronary artery stenting, transient ischemic attack, cerebrovascular accident, angina, congestive heart failure, or ventricular rhythm disturbances, they should be cleared by a cardiologist prior to participation. 12. Is of legal age and capable of providing consent 13. Is fluent in speaking, reading and understanding English
Exclusion Criteria	**General Exclusion Criteria:** 1. Has a history of 1 or more episodes of severe hypoglycemia, which resulted in any the following during the 6 months prior to Screening: a. Medical assistance (i.e. Paramedics, Emergency Room (ER) or Hospitalization) b. Coma c. Seizures 2. Has been hospitalized or has visited the ER in the 6 months prior to Screening resulting in a primary diagnosis of uncontrolled diabetes 3. Has had Diabetic Ketoacidosis (DKA) in the 6 months prior to Screening. 4. Is unable to tolerate tape adhesive in the area of sensor placement 5. Has any unresolved adverse skin condition in the area of sensor placement (e.g., psoriasis, dermatitis herpetiformis, rash, Staphylococcus infection) 6. Women of child-bearing potential who have a positive pregnancy test at Screening or plan to become pregnant during the course of the study 7. Women who are breastfeeding 8. Females who are sexually active and able to conceive will be excluded if they are not using an effective method of contraception and do not agree to continue using an effective method of contraception for the duration of the study as determined by investigator. 9. Is being treated for hyperthyroidism at time of Screening 10. Has a diagnosis of adrenal insufficiency 11. Is using hydroxyurea at time of screening or plans to use it during the study

	12. Is actively participating in an investigational study (drug or device) wherein he/she has received treatment from an investigational study drug or investigational study device in the last 2 weeks 13. Is currently abusing illicit drugs, marijuana, alcohol or prescription drugs (other than nicotine), per investigator judgement 14. Is using pramlintide (Symlin), DPP-4 inhibitor, GLP-1 agonists (as liraglutide (Victoza or other), metformin, SGLT2 inhibitors (as canagliflozin (Invokana)) at time of screening 15. Has a history of visual impairment which would not allow subject to participate in the study and perform all study procedures safely, as determined by the investigator 16. Is diagnosed with current eating disorder such as anorexia or bulimia 17. Has been diagnosed with chronic kidney disease that results in chronic anemia 18. Is on dialysis 19. Is a member of the research staff involved with executing the study.
Study Procedures and Assessments	Subjects will participate in a minimum of 7 planned study visits, as presented in **Figure 2.** If a subject is repeating participation in the study, the subject will participate in another minimum 8 planned visits**.** The description below is a high-level overview, for detailed information please see **Section 10**.

Figure 2. Study Visit Schedule Overview



Safety Assessments	All adverse events and device deficiencies will be collected and reported. A Clinical Events Committee (CEC) will be responsible for assessing all Serious Adverse Events (SAEs), Serious Adverse Device Events (SADEs), Unanticipated Serious Adverse Device Events (USADEs), Severe Hypoglycemia, Diabetic Ketoacidosis (DKA) and Deaths.
Statistical Analysis for Endpoints	Analysis will be performed by Klue Health App software release version, if applicable. **Primary Endpoints** Post-prandial Time in range (% of SG within 70-180 mg/dl) at home and In-Clinic Period will be summarized, respectively. **Safety Endpoints** Number of (S)AEs, (S)ADEs, USADEs, Severe hypoglycemic events, DKA events, and Device Deficiencies **Other Endpoints** All measurements performed by Study Period (At-Home and In-Clinic period). • Post-prandial Time in different ranges (% of SG): SG <54, 70 mg/dL, SG > 180, 250 mg/dL • Change in post-prandial % of time in euglycemia (70-180 mg/dL) for meal challenges (intervention versus baseline) • Change in post-prandial % of time in different ranges (% of SG): SG <54, 70 mg/dL, SG > 180, 250 mg/dL for meal challenges (intervention versus baseline) • 24 hour Time in range (% of SG within 70-180 mg/dl) • 24 hour Time in different ranges (% of SG): SG <54, 70 mg/dL, SG >180, 250 mg/dL • Number of Events, Area Under Curve (AUC) and Time in the hyperglycemic range: sensor glucose (SG) >180, 250 mg/dL • Number of Events, AUC and Time in the hypoglycemic range: SG < 54 and 70 mg/dL • Time spent in Auto Mode versus time spent in Manual Mode • Change of Total Daily Dose (TDD) of insulin from baseline to EOS Period • Change in BG values during meal challenge (BG prior and BG 2 hours after meal) • Insulin delivery at postprandial: Total unit of insulin in first 15 minutes, 60 minutes, 120 minutes, and 240 minutes postprandial • Subgroup analysis by type of meals • Between period analyses of all above (At-Home vs. In-Clinic)

	Subject Feedback • Descriptive summary will be used to characterize study questionnaire
Final Report	A final report will be generated once all subjects have completed the study period. Descriptive endpoints and safety data will be summarized and presented in the final report.

4. Introduction

4.1 Background

In patients with insulin dependent diabetes mellitus, glycemic control is influenced by numerous factors, such as insulin dosage, insulin absorption, timing, physiological/ lifestyle factors such as exercise, food intake, hormones and illness. These factors may contribute to significant variability in insulin requirements, which makes self-management of type 1 diabetes challenging.

Patients who are using continuous glucose monitoring, including sensor-augmented pump therapy, experience improvements in glycemic control. Advanced features of sensor-augmented pump therapy are now being used in clinical practice; these include automatic suspension of insulin delivery when a pre-set glucose threshold is reached (low glucose suspend) or is predicted to be reached (predictive low glucose suspend). Both approaches have shown that a significant reduction in the risk and burden of hypoglycemia can be achieved, especially in patients who are prone to experiencing hypoglycemia.

Medtronic's latest system is the MiniMed 780G system, also referred to as the Advanced Hybrid Closed Loop (AHCL) system, a self-adjusting basal insulin pump with autocorrection dosing. Patients using the MiniMed 780G system are not required to confirm sensor glucose using a self-monitored blood glucose (SMBG) measurement before making therapy adjustments based on displayed sensor glucose values. Patients are still required to enter manual meal announcements (grams of carbs). With burden reduction in mind, the next generation of the AHCL system is focused on automated meal gesture dosing thereby eliminating the need for manual meal announcements.

Meal gesture dosing is a mode whereby meal announcements are not entered manually by the user. Instead, when meal gesture dosing is active, meal announcements are generated automatically by the system based on the detection of eating gestures. Eating gestures are derived from analyzing the motion sensor data from the user's Apple Watch (worn on the user's hand of eating). When eating is detected, the system translates the detected eating activity into an equivalent carb amount and sent to the pump as a meal announcement. Sensor glucose based safety guardrails and rate control help ensure that automatic generation of meal announcements is safe.

4.2 Purpose

The purpose of this study is to evaluate subject safety of using the Klue Health app utilizing meal gesture micro insulin dosing (meal gesture dosing) within the AHCL system in adult subjects with type 1 diabetes adult subjects in a clinic setting.

5. Objectives and Endpoints

5.1 Objectives

The objective of the study is to collect data for meal gesture dosing for unannounced meals within the AHCL system to be used for development of Medtronic Diabetes devices and products.

5.2 Endpoints

Analysis will be performed by Klue Health App software release version, if applicable.

5.2.1 Primary Endpoints

- Post-prandial Time in range (% of SG within 70-180 mg/dl) at home and In-Clinic Period will be summarized, respectively.

5.2.2 Safety Endpoints

- Number of (S)AEs, (S)ADEs, USADEs, Severe hypoglycemic events, DKA events, and Device Deficiencies

5.2.3 Other Endpoints

All measurements performed by Study Period (At-Home and In-Clinic period).

- Post-prandial Time in different ranges (% of SG): SG <54, 70 mg/dL, SG > 180, 250 mg/dL
- Change in post-prandial % of time in euglycemia (70-180 mg/dL) for meal challenges (intervention versus baseline)
- Change in post-prandial % of time in different ranges (% of SG): SG <54, 70 mg/dL, SG > 180, 250 mg/dL for meal challenges (intervention versus baseline)
- 24 hour Time in range (% of SG within 70-180 mg/dl)
- 24 hour Time in different ranges (% of SG): SG <54, 70 mg/dL, SG > 180, 250 mg/dL
- Number of Events, Area Under Curve (AUC) and Time in the hyperglycemic range: sensor glucose (SG) > 180, 250 mg/dL
- Number of Events, AUC and Time in the hypoglycemic range: SG < 54 and 70 mg/dL
- Time spent in Auto Mode versus time spent in Manual Mode
- Change of Total Daily Dose (TDD) of insulin from baseline to EOS Period
- Change in BG values during meal challenge (BG prior and BG 2 hours after meal)
- Insulin delivery at postprandial: Total unit of insulin in first 15 minutes, 60 minutes, 120 minutes, and 240 minutes postprandial
- Subgroup analysis by type of meals
- Between period analyses of all above (At-Home vs. In-Clinic)

5.2.4 Subject Feedback

- Descriptive summary will be used to characterize study questionnaire results

6. Study Design

This study is a single-center, single arm study in adult subjects with type 1 diabetes utilizing AHCL System with meal gesture detection and micro dosing (meal gesture dosing). Meal gesture dosing is a mode whereby meal announcements are not entered manually by the user. Instead, when meal gesture dosing is active, meal announcements are generated automatically by the system based on the detection of eating gestures and micro doses of insulin are given. See **Figure 3** for an overview.

Overall subject participation will be approximately 3 weeks to 6 months.

- A total of up to 40 subjects (aged 18-75) may be enrolled at one investigational center in Israel to have at least 16 subjects complete the study. Subjects may repeat participation at the request of the Sponsor and at the discretion of the investigator but will only be counted once toward the total number of subjects.

6.1 Duration

The study is anticipated to last approximately 15 months from investigational center initiation to finalization of all data entry and monitoring procedures. Individual subject participation (per study participation) is expected to be approximately 3 weeks to 6 months.

6.2 Rationale

Clinical evidence is required to evaluate meal gesture dosing for unannounced meals as the next step in the development of the AHCL system. Additionally, the study will collect biometric data for a novel, non-invasive, wearable band.

7. Product Description

7.1 General Overview of the AHCL System with Meal Gesture Dosing

The AHCL system with Meal Gesture Dosing evaluated in this study includes a commercial/CE-Marked insulin pump with investigational software and both CE-marked and investigational components, which will all be used as described in labelling and instructions for use for which CE mark has been obtained (as applicable). The AHCL system will also include the addition of the Klue Health mobile app with investigational software (installed on Apple Watch) for meal gesture detection and micro dosing. The AHCL system without meal gesture dosing is indicated for management of type 1 diabetes.

Figure 2. AHCL System with Meal Gesture Dosing

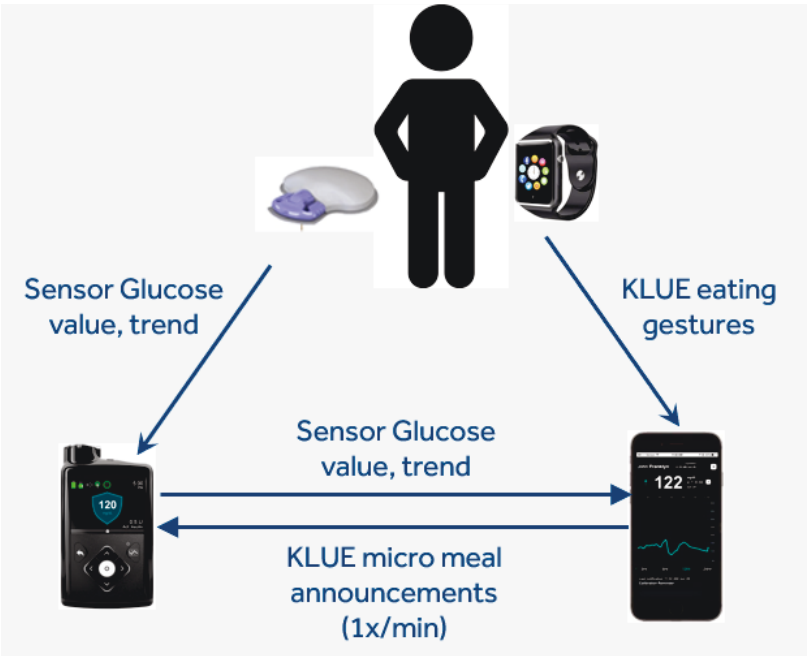


Table 1. Status of Study Product and Consumables*

Device Name	MDT Model number/ part number	Device Status
MiniMed 780G Insulin Pump, with investigational software version 1.0W.1003	MMT-1886 / MMT-1896WW (Kit)	Investigational**
Guardian Link 3 Transmitter*	MMT-7910NA	Investigational
Klue™ Health App, with investigational software release tag 1.0	N/A	Investigational
Klue™ Health App, with investigational software release tag 2.0	N/A	Investigational
Roche Accu-Chek Guide Link Glucose Meter with modification to allow communication with study pump	04015630067671	Investigational
Roche Accu-Chek Guide Link Glucose Meter	08116083022	Non-Investigational/CE-Marked
MiniMed Clinical App, with software version 1.1.1	MMT-6104 (iOS)	N/A, not considered medical device
CareLink Clinical App, with software version 1.1.2	MMT-6114 (iOS)	N/A, not considered medical device
Guardian Sensor 3	MMT-7020C1	Non-Investigational/CE Marked
Charger*	MMT-7715	Non-Investigational/CE Marked
Tester*	MMT-7736L	Non-Investigational/CE Marked
One-press Serter*	MMT-7512W	Non-Investigational/CE Marked

Device Name	MDT Model number/ part number	Device Status
Apple Watch	N/A	N/A, not considered medical device
Apple iPhone	N/A	N/A, not considered medical device
CareLink System	MMT-7350	Non-Investigational/CE Marked
CareLink Personal	MMT-7333	Non-Investigational/CE Marked
Other compatible commercially available Roche glucose meter	N/A	Non-Investigational/CE Marked
FreeStyle Optium Neo	N/A	Non-Investigational/CE Marked
Consumables and Accessories	See **Appendix 18.5**	Non-Investigational/CE Marked
[redacted]	[redacted]	N/A, not considered medical device
[redacted]	N/A	N/A, not considered medical device

*Devices may be combined and distributed in kits

**Pump is CE Marked but the software has been updated

***Refer to user guides and IFU for a list of the materials in contact with the human tissue/body fluid

Table 2. Indicative Number of Devices Per Subject Participation During the Study

Item	Units per Subject Participation
MiniMed 780G insulin pump, with investigational software version 1.0W.1003	1
Guardian Link 3 Transmitter	1
Guardian Sensor (3)	5*
One-press Serter	1
Apple Watch™	1
Apple iPhone™	1
Reservoirs (boxes of 10)	1*box of 10
Infusion Sets (boxes of 10)	1*box of 10
Infusion Set Serter (if applicable)	1
AA Alkaline Battery	4
Roche Accu-Chek Guide Link Glucose Meter with modification to allow communication with study pump or other compatible commercially available Roche glucose meter	1
Roche Accu-Chek Strips	75*
FreeStyle Optium Neo	1
[redacted]	1
[redacted]	1

*If run-in phase is extended up to 3 months, sufficient quantities of consumables will be provided to subject accordingly.

7.1.1 Investigational Devices

7.1.1.1 MiniMed 780G Insulin Pump

The MiniMed 780G Insulin Pump houses electronics, a pumping mechanism, a user interface, and a medication reservoir within the same physical device. The pump communicates via Bluetooth® Low Energy wireless communication protocol with the compatible devices in the MiniMed 780G System: Guardian Link 3 Transmitter, Roche's Accu-Chek Guide Link Blood Glucose Meter, consumer electronic devices with the CareLink system software.

The most notable enhancements to the MiniMed 780G System are the incorporation of modifications to the closed loop algorithm that includes the addition of adjustable target setpoints (100 mg/dL, 110 mg/dL and 120 mg/dL), an auto correction bolus without user input or acknowledgement and fine tuning of safeguards in order to reduce auto mode exits and improve the user experience.

In this study, the MiniMed 780G Pump will interact with the following devices:

- The MiniMed 780G Pump receives the sensor glucose values and sensor integrity check from the Guardian Link 3 Transmitter which is connected to the Guardian Sensor 3.
- The MiniMed 780G Pump receives blood glucose values from the Roche's Accu-Chek Guide Link blood glucose meter
- In addition, the MiniMed 780G Pump transmits data to a compatible consumer electronic device with the MiniMed Clinical app, to provide a secondary display for passive monitoring of CGM and pump data for the user.
- The MiniMed 780G Pump also transmits data to CareLink system through the MiniMed Clinical app.
- The MiniMed 780G Pump firmware has been modified which makes the firmware and pump investigational within the study. The pump will transmit SG values and trends to the Klue Health App and to accept micro-meal announcements from the Klue Health App. Such micro-meal announcement is treated by the pump in the same way as a manual meal announcement entered by the user. To allow the Klue Health App to communicate with the pump, the pump firmware as well as the Klue Health App have been modified to create a direct data interface. The data interface piggybacks on a secure Bluetooth Low Energy connection established by the MiniMed Clinical App.

7.1.1.2 Guardian Link 3 Transmitter

The Guardian Link 3 transmitter is a device that reads the electronic signal generated by the sensor. In addition, the transmitter contains a custom Application Specific Integrated Circuit (ASIC), which enables Electrochemical Impedance Spectroscopy (EIS). The EIS measurements are used as diagnostics for the sensor, which are incorporated into the sensor calibration logic.

In addition, the transmitter also contains the sensor calibration algorithm which converts the sensor signal to a SG value using calibration BG values from a meter relayed to the transmitter through the pump. The transmitter transmits the calculated glucose data to the pump via Bluetooth Low Energy. Some elements of the calibration logic include prompting the user to calibrate when needed, referred to as "Smart Cal," instead of strictly scheduled time-based calibration requirements. The algorithm is designed to improve and optimize performance when paired with the sensors. In this study, the

Guardian Link 3 transmitter will be connected to the Guardian Sensor (3). Data will be transmitted to the pump which transmits data to the CareLink system via upload through the MiniMed Clinical app. The transmitter has been updated to make it compatible with other components.

7.1.1.3 Klue Health App

The Klue Health app (installed on the Apple Watch) communicates with the Apple Watch for meal gesture detection. It analyzes motion sensor data from the user's Apple Watch (worn on the user's hand of eating) to detect eating and drinking gestures. The information collected by Klue is stored on the Klue data cloud.

The Klue Health app includes investigational software that, from detected eating gestures, determines an appropriate carb amount to be transmitted to the MiniMed 780G Pump as a micro-meal announcement. SG-based safety guardrails and rate control help ensure safety of the automated micro-meal announcements. In this study, The Klue Health app with investigational software release tag 1.0 should be used until investigational software release tag 2.0 becomes available which contains updates to meal bolusing

7.1.1.4 Roche Accu-Chek Guide Link Glucose Meter with modification to allow communication with study pump

The Roche's Accu-Chek Guide Link meter is a home blood glucose meter designed to measure and transmit blood glucose (BG) values to the compatible insulin pumps via a Bluetooth Low Energy wireless communication protocol. The insulin pump then sends the BG values to the transmitter for calibration of the glucose sensor. The transmission of BG values from a compatible meter is an optional feature provided as a convenience to the user; it eliminates the need to manually enter BG values into the pump. The Accu-Chek Guide Link blood glucose meter a is compatible with Roche's Accu-Chek test strips.

The Roche's Accu-Chek Guide Link meter used in this study is similar to the commercial device except that the study meter has been modified to allow pairing with the study pumps only (with a specific engineering SAKE key). All functionalities remain the same. In this study, the modified/investigational Roche meter will be used, pending study supply.

7.1.2 Non-Investigational Product

The following non-investigational devices designated for use in the study are described in this section. These devices are all CE-marked and will be used within their intended use according to the labelling and instructions for use.

7.1.2.1 Guardian Sensor 3

The Guardian Sensor 3 glucose sensor, referred to as Guardian Sensor 3 in this protocol, is a sensor that contains one microelectrode with a thin coating of glucose oxidase beneath several layers of biocompatible membrane. The sensor is the latest generation of glucose sensor with design changes supporting improved accuracy. It is intended to penetrate the skin at a 90-degree angle. The sensor is tubeless. An introducer needle penetrates the skin surface and provides support for the sensor microelectrode during insertion. The sensor continuously converts small amounts of glucose from the subject's interstitial fluid into an electronic signal that is received by a transmitter or recorder, the

strength of which is proportional to the amount of glucose present in the blood. The electrode is composed of embedding, signal-conducting and insulating layers.

7.1.2.2 One-press Serter

The One-press Serter, referred to as the Serter in this protocol, is an insertion device that is used to ensure correct placement of the Guardian Sensor 3 into the user's subcutaneous tissue. Insertion is triggered when the two spring loaded buttons on the sides of the Serter are pressed simultaneously. The Serter is intended as a single patient, non-sterile, multi-use device.

7.1.2.3 Charger

The Charger is used to recharge the Guardian Link 3 transmitter as needed. A fully charged battery provides up to 7 days of Guardian Link 3 transmitter use. The system includes a battery charger that will recharge the device according to the user guide.

7.1.2.4 Tester

The Tester operates as a sensor simulator creating signal current at a level that is within the range of an in-vivo sensor during normal operation.

7.1.2.5 CareLink Personal Software

Medtronic CareLink Personal software is an internet-based software system which allows the device data to be uploaded and reviewed by the subject. The CareLink Personal software allows subjects to upload data from Medtronic MiniMed insulin pumps and a range of system-supported, third-party BG meters. The data contained in CareLink Personal software is accessible to users using a standard browser, i.e., Microsoft® Internet Explorer or Google Chrome, on an Internet enabled personal computer (PC).

The CareLink Personal software use standard Transport Layer Security (TLS) technology. TLS transmission protocol invokes encryption on both ends of the transmissions and is the standard for all security-based systems. The encryption remains in effect whether the data is moving to and from the client and server in the United States, or to and from a client in another country to the United States. The data is secure behind a three-tier industry standard architecture, which places the database behind three different firewalls, where each firewall separates a tier:

- The internet to the web server;
- Web server to the application server;
- Application server to the database server.

7.1.2.6 CareLink System Software

Medtronic CareLink system software is an internet-based software system which allows the device data to be uploaded, viewed and easily evaluated by the physician. The CareLink system software allows retrospective review of device data and was developed for use by the investigational center staff. The CareLink system software allows the investigational center staff to manage, create, and request for approval to link the subject's account. The data contained in CareLink system software is accessible to

users using a standard browser, i.e., Microsoft® Internet Explorer or Google Chrome, on an Internet enabled PC.

The CareLink system software use standard TLS technology. TLS transmission protocol invokes encryption on both ends of the transmissions and is the standard for all security-based systems. The encryption remains in effect whether the data is moving to and from the client and server in the United States, or to and from a client in another country to the United States. The data is secure behind a three-tier industry standard architecture, which places the database behind three different firewalls, where each firewall separates a tier:

- The internet to the web server;
- Web server to the application server;
- Application server to the database server.

7.1.2.7 FoodPrint App

The FoodPrint app by Nutrino is a meal and event logging app. It lets the user take pictures of a meal which are synced with the food diary. FoodPrint can also be used to log activity, sleep, medications, blood glucose, and insulin. In this study, subjects will log:

- Only baseline meal challenges and activity during the at-home study period
- All meals and activity during the in-clinic study period

7.1.2.8 MiniMed Clinical App

The MiniMed Clinical app is an optional accessory which receives pump data via Bluetooth Low Energy wireless communication from the pump. The MiniMed Clinical app provides users with the convenience to wirelessly transfer pump data to CareLink Personal/CareLink system software and also provides a mirroring display of the pump screen. The MiniMed Clinical app is not designed to control or monitor the performance of the insulin pump nor for direct monitoring of pump data. As a mirroring display, the app can provide alerts to the subject via the user interface. All alerts must be addressed on the insulin pump. In this study, the app will be installed on the iPhone (software has been updated to make it compatible with study devices). The MiniMed Clinical app is not considered a medical device.

7.1.2.9 CareLink Clinical App

The CareLink Clinical app is an optional accessory which receives pump data wirelessly from the CareLink server. The CareLink Clinical app provides a mirroring display of the MiniMed Clinical app screen, for remote monitoring by a care partner (i.e. caregiver or healthcare provider). As a mirroring display, the app can provide notifications to the care partner via the user interface. The CareLink Clinical app is not considered a medical device.

7.1.2.10 Apple Watch

The Apple Watch is a commercially available wearable smartwatch that allows users to perform various activities. In this study, the Klue Health app (iOS app compatible with Apple Watch) will be installed and subjects will wear the smartwatch on the wrist of the hand used for eating. When the Klue Health app is

active, the Klue watch face will take over the default Apple Watch face. Subjects shall not use the Apple Watch Workout app during the study.

7.1.2.11 Apple iPhone

In this study, apps will be pre-loaded onto a sponsor-provided smartphone prior to subject's use.

7.1.2.12 FreeStyle Optium Neo

The FreeStyle Optium Neo Blood Glucose & Ketone Monitoring System, referred to as ketone meter throughout this protocol, can measure both blood glucose (sugar) and blood ß-Ketone. In this study, however, the meter will only be used to measure ß-Ketone levels, which will be collected for reporting and review (see Investigator/Coordinator binder for details) and as described in the body of this study protocol. This particular meter will be used because it is the only commercially available meter which allows quantification of blood ß-Ketone levels and is the preferred patient method of testing over urine testing.

Note: In the event the blood ketone meter is not used to collect ketone values, urine ketones must be measured and entered into CareLink system instead (if available at the time of the study).

7.1.2.13 Roche Accu-Chek Guide Link Glucose Meter or other compatible commercially available Roche glucose meter

The Roche's Accu-Chek Guide Link meter is a home blood glucose meter designed to measure and transmit blood glucose (BG) values to the compatible insulin pumps via a Bluetooth Low Energy wireless communication protocol. The insulin pump then sends the BG values to the transmitter for calibration of the glucose sensor. The transmission of BG values from a compatible meter is an optional feature provided as a convenience to the user; it eliminates the need to manually enter BG values into the pump. The Accu-Chek Guide Link blood glucose meter a is compatible with Roche's Accu-Chek test strips. In this study, a commercial Roche meter will be used only if the modified/investigational Roche meter is unavailable. If used, it will require the subject to manually enter BG values into the pump.

7.1.3 [redacted]

7.1.4 [redacted]

- Battery status
- Alert to reposition the wearable band if the signal strength is poor
- Alert that band is out of Bluetooth Low Energy range

This application is exclusively for clinical investigations and does not present data or therapy recommendations to the user. [redacted]

7.2 Consumable Devices

Infusion sets, reservoirs, infusion set serter devices, glucose meter accessories and other consumable materials will be provided to subjects for use in the study. See **Appendix 18.5.**

7.3 Packaging

The labelling of the Investigational devices and CE marked devices will be provided in accordance with local language requirements. The outer packaging of the Investigational devices will be labelled “For clinical trial use only” and as required by national regulations, in local language(s) of the participating country.

7.4 Insulin

Subjects will use their own rapid-acting analogue insulin (Novolog™ [aspart insulin] or Humalog™ [lispro insulin]) during this study.

7.5 Anticipated Device Changes

There are no changes anticipated for any of the devices during the course of the study.

7.6 Product Accountability

Good clinical research practice requires that investigators and research teams ensure accurate accountability for any investigational device used in a research trial. It is expected that all investigational devices will be used in the manner intended during the study and that they will be used only by (on) subjects who have consented to participate in the research study and by investigational center staff trained on the study.

Any investigational devices being used in clinical research must be strictly accounted for and will not be shipped to any investigational center unless all of the necessary approvals (e.g., regulatory authority and EC) have been received.

The principal investigator or an authorized designee shall keep records documenting the receipt, use, return and disposal of the investigational devices. Additional details regarding device accountability and device disposition requirements are provided in **Table 3**.

Table 3. Device Accountability Requirements

Device	Record on Site Received eCRF	Record Disbursement, Returned or Not Returned from Subject on Subject Device Identification eCRF	Subject Return Device to Investigational Center	Record Returned or Not Returned to Sponsor on Site Returned eCRF	Site Return Device to Sponsor at Conclusion of Study
MiniMed 780G Insulin Pump, with investigational software version 1.0W.1003, MMT-1886 / MMT-1896WW (Kit)	Yes	Yes	Yes	Yes	Yes
Guardian Sensor 3, MMT-7020C1	No	No	No	No	Dispose or return unused to sponsor
Guardian Link 3 Transmitter, MMT-7910NA	Yes	Yes	Yes	Yes	Yes
Roche Accu-Chek Guide Link Study Meter with modification to allow communication with study pump, 04015630067671	Yes	Yes	Yes	Yes	Yes
Roche Accu-Chek Guide Link Study Meter, 08116083022 (or other compatible commercially available Roche glucose meter)	Yes	Yes	Yes	Yes	Dispose or return unused to sponsor
FreeStyle Optium Neo Ketone Meter	No	No	Yes	No	Dispose or return unused to sponsor
Apple iPhone	Yes	Yes	Yes	Yes	Yes
Apple Watch	Yes	Yes	Yes	Yes	Yes
[redacted]	Yes	Yes	Yes	Yes	Yes

7.6.1 Receipt and Inventory of Study Devices by Investigational Center

- Upon receipt of the study devices, investigational center staff must check the inventory of the shipment, making sure that information on the packing slips/invoices matches exactly the contents of the containers, as applicable, including:
  - Ship to Address
  - Reference Number
  - Device Type
  - Quantity
  - Quantity per package
  - Lot number (where applicable)
  - Serial number (where applicable)

- Ensure that devices and supplies received have not reached or exceeded their expiration date, then sign and date the packing slip/invoice, noting any discrepancies, send a copy to the Medtronic Study Team as an Acknowledgement of Receipt and file in appropriate study binder. Notify the Medtronic Study Team of any discrepancies.

7.6.2 Storage of Study Devices at Investigational Center

Study devices are to be stored in a secure environment with access limited to authorized research personnel. Study devices are stored in the appropriate environmental conditions as identified in the IFU/labelling.

7.6.3 Disbursement of Study Devices

Each time a serialized study device is disbursed to a subject by the investigator or authorized member of the research team, all required eCRF and source documentation will be completed (see **Table 3**). Documentation may include:

- Date of disbursement
- Subject ID
- Serial Number
- Amount dispensed

7.6.4 Return or Disposal of Study Devices

After use by the subject, the investigational center is expected to accept and retain all devices as described in **Table 3. Device Accountability Requirements** and store them in a secure environment. If containers/units/devices are missing, the reasons should be documented. If discrepancies between the amounts used by subjects and the amounts expected to be returned exist, the reasons should be documented.

Requirements for return of devices by subjects to the investigational center and return of device by the investigational center to the sponsor are listed in **Table 3**. The devices that are being returned to the investigational center may be returned to the sponsor as subjects complete the study, at study closure or upon sponsor request.

Other unused consumable devices (as listed in **Appendix 18.5**), will be disposed of appropriately by investigational center staff.

Disposable and consumable devices that have been used by a subject will be disposed of appropriately by the subject or the investigational center staff during the conduct of the study.

All study devices that are required to be entered into the study database must be accounted for as described above before they are returned to the sponsor.

7.7 Device Re-Use Disclosure

The durable devices in this study may be re-used. The site will clean the devices prior to redistributing per IFUs.

8. Study Site Requirements

8.1 Investigator/Investigational Center Selection

See **Section 16.1** for details regarding investigator section and qualification.

8.2 Study Site Activation

During the activation process (prior to subject enrollment), Medtronic will train investigational center staff. If new members join the study investigational center team, they will receive training on the applicable study requirements relevant to their role before contributing to the study.

Prior to performing study related activities, all regulatory authority requirements shall be fulfilled, including but not limited to the following:

- EC approval (and voting list, as required by local law) of the current version of the CIP and Informed Consent Form (ICF)
- Regulatory authority approval or notification (as required per local law)
- Fully executed CTA
- Financial disclosure
- CV of investigators
- Documentation of delegated tasks
- Documentation of study training

In addition, all participating investigational center staff must be trained on the current version of the CIP as well as on the applicable study requirements depending on their role and must be delegated by the principal investigator prior to performing delegated study activities.

Medtronic will provide the investigational center with documentation of investigational center/investigator subject enrollment readiness; this letter must be received prior to subject enrollment.

9. Selection of Subjects

9.1 Study Population

A total of up to 40 adult subjects (aged 18-75) with type 1 diabetes will be enrolled at one investigational center in Israel to have at least 16 subjects complete the study. Subjects who are repeating the study will be counted once towards the total amount of subjects.

9.2 Subject Enrollment

Subjects will be considered enrolled in the study upon signing the ICF. A subject will be assigned a unique study subject identification (SID) via the eCRF, which is a 9-digit code (339-XXX-XXX). The first three digits refer to the CIP number (339), the next three digits refer to the investigational center number, and the last 3 digits refer to the subject number assigned during Visit 1 (e.g., 339 002001 is subject 001 from site 002).

The investigator will maintain a log of all subjects enrolled in the clinical study, assigning a SID linked to their names, alternative subject identification and contact information.

9.3 Inclusion Criteria

A subject who meets any of the following criteria will be excluded from participation in this study:

1. Is age 18-75 years at time of screening
2. Has a clinical diagnosis of type 1 diabetes for 2 years or more as determined via source documentation
3. Pump therapy for greater than 6 months prior to screening
4. Real-time continuous glucose monitoring (RT-CGM) experience greater than 3 months prior to screening
5. Must have a minimum daily insulin requirement (Total Daily Dose) of greater than or equal to 8 units
6. Is willing to perform ≥2 fingerstick blood glucose measurements daily
7. Is willing to perform required sensor calibrations
8. Is willing to wear the system continuously throughout the study
9. If subject has celiac disease, it has been adequately treated as determined by the investigator
10. If the subject has had any of the following cardiovascular events more than 1 year prior to of screening: myocardial infarction, unstable angina, coronary artery bypass surgery, coronary artery stenting, transient ischemic attack, cerebrovascular accident, angina, congestive heart failure, or ventricular rhythm disturbances they should be cleared by a cardiologist prior to participation, if deemed necessary by the investigator.
11. If the subject has had any of the following cardiovascular events within 1 year of screening: myocardial infarction, unstable angina, coronary artery bypass surgery, coronary artery stenting,

transient ischemic attack, cerebrovascular accident, angina, congestive heart failure, or ventricular rhythm disturbances, they should be cleared by a cardiologist prior to participation.

12. Is of legal age and capable of providing consent
13. Is fluent in speaking, reading and understanding English

9.4 Exclusion Criteria

Subjects will be considered included in the study, if they meet all the following criteria and none of the exclusion criteria:

1. Has a history of 1 or more episodes of severe hypoglycemia, which resulted in any the following during the 6 months prior to Screening:
    a. Medical assistance (i.e., Paramedics, Emergency Room (ER) or Hospitalization)
    b. Coma
    c. Seizures
2. Has been hospitalized or has visited the ER in the 6 months prior to Screening resulting in a primary diagnosis of uncontrolled diabetes
3. Has had Diabetic Ketoacidosis (DKA) in the 6 months prior to Screening.
4. Is unable to tolerate tape adhesive in the area of sensor placement
5. Has any unresolved adverse skin condition in the area of sensor placement (e.g., psoriasis, dermatitis herpetiformis, rash, Staphylococcus infection)
6. Women of child-bearing potential who have a positive pregnancy test at Screening or plan to become pregnant during the course of the study
7. Women who are breastfeeding
8. Females who are sexually active and able to conceive will be excluded if they are not using an effective method of contraception and do not agree to continue using an effective method of contraception for the duration of the study as determined by investigator.
9. Is being treated for hyperthyroidism at time of Screening
10. Has a diagnosis of adrenal insufficiency
11. Is using hydroxyurea at time of screening or plans to use it during the study
12. Is actively participating in an investigational study (drug or device) wherein he/she has received treatment from an investigational study drug or investigational study device in the last 2 weeks
13. Is currently abusing illicit drugs, marijuana, alcohol or prescription drugs (other than nicotine), per investigator judgement
14. Is using pramlintide (Symlin), DPP-4 inhibitor, GLP-1 agonists (as liraglutide (Victoza or other), metformin, SGLT2 inhibitors (as canagliflozin (Invokana)) at time of screening
15. Has a history of visual impairment which would not allow subject to participate in the study and perform all study procedures safely, as determined by the investigator
16. Is diagnosed with current eating disorder such as anorexia or bulimia
17. Has been diagnosed with chronic kidney disease that results in chronic anemia

18. Is on dialysis
19. Is a member of the research staff involved with executing the study.

10. Study Procedures

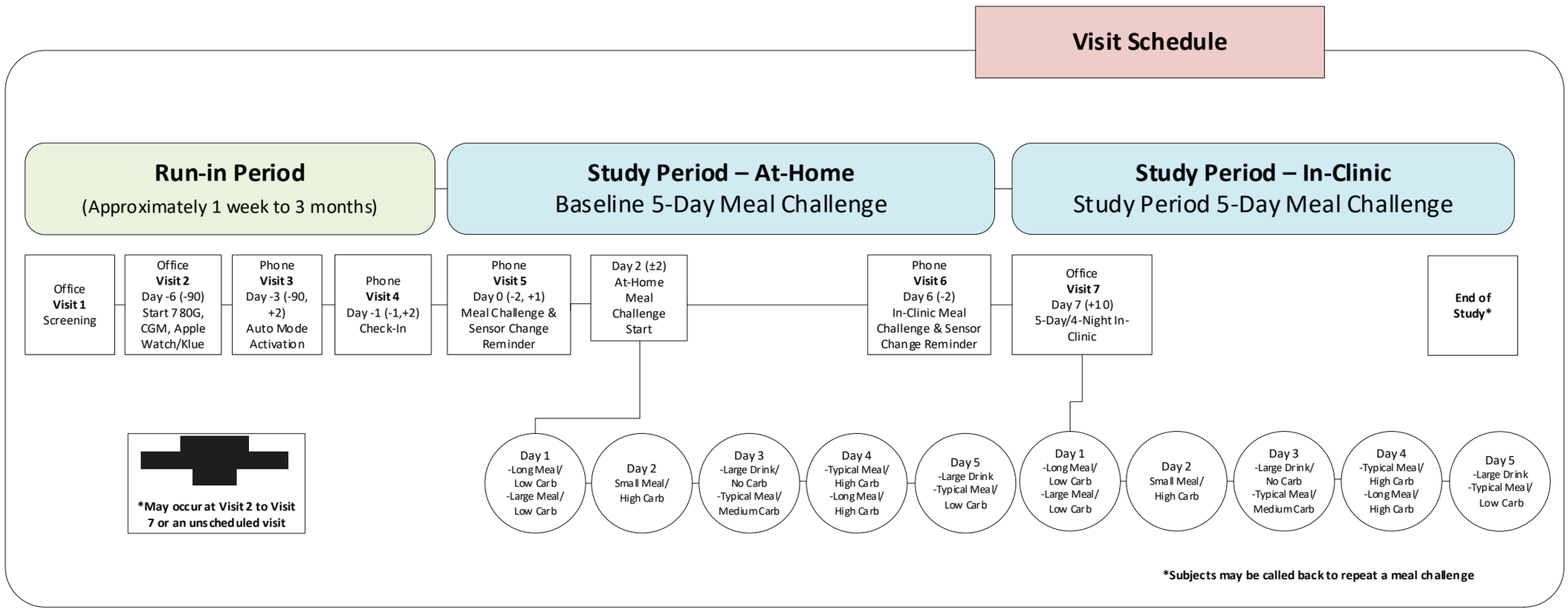
The section below describes the study procedures that the subject will undergo during the clinical study.

10.1 Schedule of Events

Subjects will participate in a minimum of 8 planned study visits as presented in **Figure 3** or approximately 3 weeks to 6 months of device wear. If a subject is repeating participation in the study, the subject will participate in another minimum 8 planned visits**.** Refer to **Table 4** for additional visit details.

If subject ends the study early (i.e. before their last scheduled visit), all requirements that apply to the final visit should be completed if possible.

Figure 3. Visit Schedule



The study is comprised of a run-in period of approximately 1 week to 3 months and a study period of approximately 10 days.

Prior to study start, Investigator or authorized designee must obtain written informed consent from the patient before any clinical study related activity (including screening) takes place and document informed consent process in the medical chart of the patient (refer to **Section 10.11 Subject Consent**).

Study staff will discuss with the participant the visit schedule and will make arrangements with the subjects for the contacts at investigational center and sponsor. Participants who are not compliant with the arranged contacts, which may impact patient's safety, may be discontinued at the discretion of the investigator.

Subjects will be using the Klue Health app and Apple Watch. The subject must wear the Apple watch on the wrist of the hand used for eating for the duration of the study.

Subjects will also be using the [redacted]

Run-in Period (approximately 1 week to 3 months in total after starting devices):

The run-in period is intended to allow subjects to become familiar with the new study devices, while using the same insulin they will be using during the study period.

For the duration of the at-home run-in period and the at-home study period (baseline meal challenges, see details below), study subjects will be using the study pump with SmartGuard Auto Mode turned ON (after warm-up period).

For the run-in period, The Klue Health app will be configured in monitoring-only mode. The subject must wear the Apple watch on the wrist of the hand used for eating.

Study Period – At-Home: Baseline Meal Challenge

Study subjects will undergo a 5-day meal challenge at specific meal(s) on each day.

5 days of baseline meal challenges at home:

- Day 1: long meal with low carb count (lunch) and large meal with low carb count (dinner)
- Day 2: small meal with high carb count (lunch)
- Day 3: large drink with no carbs (breakfast) and typical meal size with medium carb count (dinner)

- Day 4: long meal with high carbs (lunch)
- Day 5: large drink with high carbs (breakfast) and typical meal size with low carb count (lunch)

For the baseline meal challenges, study subjects will be asked by investigational center staff to eat a pre-defined meal, while bolusing using the pump's bolus calculator (manually announcing the meals) and logging the challenge meals in the FoodPrint app. For all other meals, subjects can consume their usual meals, but meals do not need to be logged in FoodPrint.

The Klue Health app should remain configured in monitoring-only mode during this time. The subject must wear the Apple watch on the wrist of the hand used for eating.

Study Period – 5 days (4 nights) In-Clinic:

After the run-in period and completion of the 5-day at-home study period with baseline meal challenges, study subjects will check into the clinic for a 5-day (4 nights) intervention.

Study subjects will be asked by investigational center staff to consume meals of the same size and content they consumed for the meal challenges during the baseline meal challenge (at-home study period). For example: If a large sized dinner meal with low carbohydrate content was consumed at 5 pm on Day 1 during the baseline meal challenge, that same dinner meal should be consumed at approximately the same time on Day 1 of the in-clinic study period. Subjects will be asked by investigational center staff to check BG at the start of the meal, as well as 2 hours and 4 hours after the start of the meal and provide correction as necessary. All meals consumed during the in-clinic study period should be logged in the FoodPrint app.

Subjects will be instructed by investigational center staff to not use the pump's meal bolus calculator (no manual meal announcements) for the duration of the intervention.

Scheduled meal challenges during the study period (mirror baseline meal challenge):

- Day 1: long meal with low carb count (lunch) and large meal with low carb count (dinner)
- Day 2: small meal with high carb count (lunch)
- Day 3: large drink with no carbs (breakfast) and typical meal size with medium carb count (dinner)
- Day 4: long meal with high carbs (lunch)
- Day 5: large drink with high carb (breakfast) and typical meal size with low carb count (lunch)

On Day 5 of the in-clinic meal challenge, a subject may be asked to repeat a specific meal challenge which may require the subject to participate for an additional day.

10.2 Study Start and Run-In Phase

10.2.1 Visit 1: Consent and Screening

The investigational center staff will:

- Obtain written informed consent
- Determine if subject meets eligibility criteria (**Sections 9.3 and 9.4**)
- Collect demographic information
- Review subject's medical history
- Measure/Collect height and weight

10.2.2 Visit 2: Start Run-In (Office), Day -6 (window of -90 days)

The investigational center staff will:

- Dispense study devices
- Start Apple Watch with Klue Health app in monitoring mode
- Train subject on meal challenges and how to log meals/activities in FoodPrint
- Provide pump training and CGM training and start on pump system including MiniMed Clinical app
- Complete baseline subject questionnaire
- Ask subject about adverse events or device deficiencies

10.2.3 Visit 3: Phone, Day -3 (window of -90, +2 days)

The investigational center staff will:

- Train subject and have subject activate SmartGuard Auto Mode feature
- Remind subject to wear Apple watch on dominant hand used for eating
- Ask subject about adverse events or device deficiencies

10.2.4 Visit 4: Phone, Day -1 (window of -1, +2 days and may be combined with Visit 5)

The investigational center staff will:

- Check in with subject to see how pump/CGM wear is going
- Remind subject to wear Apple watch on dominant hand used for eating
- Ask subject about adverse events or device deficiencies

10.3 Study Period

10.3.1 Study Period – At-Home: Baseline Meal Challenge

10.3.1.1 Visit 5: Phone, Day 0 (window of -2 day, +1 days)

The investigational center staff will:

- Remind subjects to do baseline meal challenge and to change sensor prior to starting baseline meal challenges
- Ask subjects about adverse events or device deficiencies

10.3.1.2 Baseline Meal Challenges, Day 2 (window of ±2)

- Day 1:
  - Long meal with low carbohydrate count (lunch): A meal of at least 30 minutes with many bites of food (less than 5 minutes between bite) that is smaller in carbohydrates than a regular lunch meal for an individual study subject.
  - Large meal with low carbohydrate count (dinner): A large meal consists of meal that is larger in size, but smaller in carbohydrates than a regular dinner meal for an individual study subject.

- Day 2:
  - Small meal with high carbohydrate count (lunch): A large meal consists of meal that is smaller in size, but higher in carbohydrate content than a regular lunch meal for an individual study subject.

- Day 3:
  - Large drink with no carbohydrate count (breakfast)
  - Typical meal size with medium carbohydrate count (dinner): A typical meal consists one that is typical in size and carbohydrate content, i.e. a regular dinner meal for an individual study subject.

- Day 4:
  - Long meal with high carbohydrate count (lunch): A meal of at least 30 minutes with many bites of food (less than 5 minutes between bite) that is higher in carbohydrates than a regular lunch meal for an individual study subject.

- Day 5:
  - Large drink with high carbohydrate count (breakfast)

- Typical meal size with low carbohydrate count (Lunch): This typical meal consists of meal that is regular in size, but lower in carbohydrate content than a typical lunch meal for an individual study subject.

10.3.1.3 Visit 6: Phone, Day 6 (window of -2 days)

The investigational center staff will:

- Remind subject to change sensor prior to starting in-clinic meal challenges
- Ask subject about adverse events or device deficiencies

10.3.2 Study Period – In-Clinic: Meal Challenge

10.3.2.1 Visit 7: Start In-Clinic, Day 7 (window of +10 days)

10.3.2.1.1 Day 1

The investigational center staff will:

- Activate automated meal gesture dosing feature in Klue Health app and confirm that system is working
- Instruct subject to eat:
  - Long meal with low carbohydrate count (lunch): A timed meal that is smaller in carbohydrates than a regular lunch meal for an individual study subject.
  - Large meal with low carbohydrate count (dinner): A large meal consists of meal that is larger in size, but smaller in carbohydrates than a regular dinner meal for an individual study subject.
- Ask subject about adverse events or device deficiencies

10.3.2.1.2 Day 2

The investigational center staff will:

- Instruct subject to eat:
  - Small meal with high carbohydrate count (lunch): A large meal consists of meal that is smaller in size, but higher in carbohydrate content than a regular lunch meal for an individual study subject.
- Ask subject about adverse events or device deficiencies

10.3.2.1.3 Day 3

The investigational center staff will:

- Instruct subject to eat:
  - Large drink with no carbohydrate count (breakfast)
  - Typical meal size with medium carbohydrate count (dinner): A typical meal consists one that is typical in size and carbohydrate content, i.e. a regular dinner meal for an individual study subject.
- Ask subject about adverse events or device deficiencies

10.3.2.1.4 Day 4

The investigational center staff will:

- Instruct subject to eat:
  - Typical meal size with high carbohydrate count (breakfast): This typical meal consists of meal that is regular in size, but higher in carbohydrate content than a typical breakfast meal for an individual study subject.
  - Long meal with high carbohydrate count (lunch): A timed meal that is higher in carbohydrates than a regular lunch meal for an individual study subject.
- Ask subject about adverse events or device deficiencies

10.3.2.1.5 Day 5

The investigational center staff will:

- Instruct subject to eat:
  - Large drink with high carbohydrate count (breakfast)
  - Typical meal size with low carbohydrate count (lunch): This typical meal consists of meal that is regular in size, but lower in carbohydrate content than a typical lunch meal for an individual study subject.
- Determine if subject needs to repeat any of the meal challenges
- Ask subject about adverse events or device deficiencies
- Complete subject questionnaire
-

10.3.2.1.6 End of Study

- Collect all study devices back from subject
- End of study

10.3.3

[redacted]

10.4 Data Collection/Visit Details

Table 4. Study Visit Details

	Run-In Period				Study Period							
	Visit 1 (Office)	Visit 2 (Office)	Visit 3 (Phone)	Visit 4 (Phone)	Visit 5 (Phone)	Visit 6 (Phone)	Visit 7 (Office)					End of Study
							Day 1	Day 2	Day 3	Day 4	Day 5	
Visit Window	**Enrollment /Screening**	**Day -6 (-90 days) Start Run-In**	**Day -3 (-90, +2 days)**	**Day -1 (-1, +2 days)**	**Day 0 (-2, +1 days)**	**Day 6 (-2 days)**	**Day 7 (+10 days)**					
Visit Activities and Data Collection												
Collect enrollment forms, e.g., Informed Consent, and forms required by local regulation	X											
Assess subject eligibility to participate in the study	X											
Measure subject height and weight Note: Body mass index (BMI) will be calculated automatically in the study database, based on height and weight measurements entered.	X											
Collect demographic and other baseline characteristics (including insulin type) according to eCRF questions	X											
Collect urine test for pregnancy from female subjects of child-bearing age or capability (Point of Care or local lab)	X											
Collect information about medical history	X											
Collect information about concomitant medications	X											
Collect/Assist with Questionnaires – Refer to Study Questionnaires Material.		X									X	
Create a new CareLink system account for the investigational center		X										
Create a CareLink Personal account for each subject and link each CareLink Personal account to the CareLink system account		X										
Set up iPhone and Apple Watch.		X										

	Run-In Period				Study Period							
	Visit 1 (Office)	Visit 2 (Office)	Visit 3 (Phone)	Visit 4 (Phone)	Visit 5 (Phone)	Visit 6 (Phone)	Visit 7 (Office)					End of Study
							Day 1	Day 2	Day 3	Day 4	Day 5	
Visit Window	**Enrollment /Screening**	**Day -6 (-90 days) Start Run-In**	**Day -3 (-90, +2 days)**	**Day -1 (-1, +2 days)**	**Day 0 (-2, +1 days)**	**Day 6 (-2 days)**	**Day 7 (+10 days)**					
• Set up e-mail feature on iPhone with provided e-mail address												
Set up Klue app with unique license code, refer to study material. • Confirm Klue Health App is working properly (keep meal gesturing feature disabled). • Instruct subject to ensure that the Apple Watch is worn on the hand that is used for eating and to make sure there is no alert stating "Looking for Phone" prior to each meal.		X										
Set up and train subjects on FoodPrint meal logging and meal challenges/activity. Subject will log: • Only 5 baseline meal challenges and activity during the at-home study period • All meals and activity during the in-clinic study period		X										
Train and start study subjects on the 780G system (insulin pump, CGM, MiniMed Clinical app and study meter). If available, the investigational study meter will be used. Pump settings will be as follow: • Active insulin time should be set to 2 hours. • The pump bolus speed rate is set to Quick rate. • The bolus increment/step size should be set to 0.025u • The Carb ratio should be set to <= 40 • The Audio settings for pump alerts should be configured to sound off and vibration on		X										

	Run-In Period				Study Period							
	Visit 1 (Office)	Visit 2 (Office)	Visit 3 (Phone)	Visit 4 (Phone)	Visit 5 (Phone)	Visit 6 (Phone)	Visit 7 (Office)					End of Study
							Day 1	Day 2	Day 3	Day 4	Day 5	
Visit Window	**Enrollment /Screening**	**Day -6 (-90 days) Start Run-In**	**Day -3 (-90, +2 days)**	**Day -1 (-1, +2 days)**	**Day 0 (-2, +1 days)**	**Day 6 (-2 days)**	**Day 7 (+10 days)**					
Train subject on diabetes management principles, such as the treatment of hyperglycemia and hypoglycemia. In addition, there will be training regarding the need to have access to oral glucose and glucagon in case of hypoglycemia.		X										
Train subject to have back up plan in place (e.g. insulin pen or syringe) in the event they are asked to revert back to their own therapy during the study or experience study pump issues (i.e. infusion set occlusion with high glucose).		X										
Train subjects on the use of the study meter to self-monitor blood glucose (SMBG) as needed for standard of care and to make treatment decisions. Refer to user guide. • If sensor glucose readings are not aligned with symptoms (e.g., if a study subject is feeling low while the sensor glucose reading is not low), use the meter to confirm blood glucose. If sensor glucose readings continue to be different from symptoms, call the study doctor		X										
Train subjects on the use of ketone meter. Instruct subjects that blood ketone testing is required every time BG is greater than 300 mg/dL (16.7mmol/L), as measured by the study meter. In the event the blood ketone meter is not used to collect ketone values, urine ketones should be measured and reported.		X										

	Run-In Period				Study Period							
	Visit 1 (Office)	Visit 2 (Office)	Visit 3 (Phone)	Visit 4 (Phone)	Visit 5 (Phone)	Visit 6 (Phone)	Visit 7 (Office)					End of Study
							Day 1	Day 2	Day 3	Day 4	Day 5	
Visit Window	**Enrollment /Screening**	**Day -6 (-90 days) Start Run-In**	**Day -3 (-90, +2 days)**	**Day -1 (-1, +2 days)**	**Day 0 (-2, +1 days)**	**Day 6 (-2 days)**	**Day 7 (+10 days)**					
Provide guidance around paracetamol (acetaminophen): Taking medications that contain paracetamol or acetaminophen, including, but not limited to fever reducers and cold medicine, while wearing the sensor, may falsely raise sensor glucose readings and result in an over-delivery of insulin, which may cause hypoglycemia. The level of inaccuracy depends on the amount of paracetamol or acetaminophen active in the body and may be different for each person. If paracetamol or acetaminophen is taken, stop the use of the medication before using SG readings to make treatment decisions. Use additional BG meter readings to confirm glucose level		X										
Provide study subject with study meter and ketone meter, including needed supplies		X										
Complete Quality Control (QC) testing of the study meter and ketone meter per respective user guide		X										
Dispense study materials (e.g., user guides and Instructions for Subject.)		X										
Dispense other study supplies as needed (e.g., alcohol swabs, adhesive remover, etc.)		X					X					
At all visits and/or between visits (if the investigational center is contacted), adjust insulin settings and insulin dose as needed		X					X					
[redacted]		X (if available)					X (if available)	X (if available)	X (if available)	X (if available)	X (if available)	

	Run-In Period				Study Period							
	Visit 1 (Office)	Visit 2 (Office)	Visit 3 (Phone)	Visit 4 (Phone)	Visit 5 (Phone)	Visit 6 (Phone)	Visit 7 (Office)					End of Study
							Day 1	Day 2	Day 3	Day 4	Day 5	
Visit Window	**Enrollment /Screening**	**Day -6 (-90 days) Start Run-In**	**Day -3 (-90, +2 days)**	**Day -1 (-1, +2 days)**	**Day 0 (-2, +1 days)**	**Day 6 (-2 days)**	**Day 7 (+10 days)**					
Train and start study subjects on [redacted] upon product availability. Refer to study material.		X (if available)	X (if available)	X (if available)	X (if available)	X (if available)	X (if available)	X (if available)	X (if available)	X (if available)	X (if available)	
Train and start study subjects on SmartGuard (Auto Mode) feature. • Use the default SmartGuard target of 100mg/dL. • Ensure that the auto correction feature is turned ON and remains ON throughout the course of the study. • Instruct subjects that they should not assume that Auto Mode is able to prevent all hypoglycemia or all hyperglycemia including diabetic ketoacidosis • While the SmartGuard feature is active, use the temp target feature if medication containing paracetamol or acetaminophen has been taken recently. Check the label of any medication to confirm whether paracetamol or acetaminophen is an active ingredient. Auto Mode should be switched OFF in the study pump or that subjects switch to manual injections if: • Hospital admission is needed for any reason • Glucose is persistently elevated (i.e., above 300 mg/dL [16.7 mmol/L]) • There is an Illness that prevents ingestion of fluids due to nausea and vomiting			X									

	Run-In Period				Study Period							
	Visit 1 (Office)	Visit 2 (Office)	Visit 3 (Phone)	Visit 4 (Phone)	Visit 5 (Phone)	Visit 6 (Phone)	Visit 7 (Office)					End of Study
							Day 1	Day 2	Day 3	Day 4	Day 5	
Visit Window	**Enrollment /Screening**	**Day -6 (-90 days) Start Run-In**	**Day -3 (-90, +2 days)**	**Day -1 (-1, +2 days)**	**Day 0 (-2, +1 days)**	**Day 6 (-2 days)**	**Day 7 (+10 days)**					
• There is an occlusion alarm with elevated glucose, where the study subject is not able to address the occlusion by changing the infusion set • There is an episode of severe hypoglycemia • There is an episode of DKA												
Confirm that subject placed the glucose sensor in a location that is approved for placement as per the User guide		X	X	X	X	X	X	X				
Enable meal gesture dosing feature in the Klue Health app. Refer to instructions.							X					
Instruct subjects not to use the Bolus Wizard feature and enter carbs for meals (make meal announcements) while meal gesture dosing feature is activated.							X					
Enter data into eCRFs as required	X	X	X	X	X	X	X	X	X	X	X	X
Collect study deviations, if applicable	X	X	X	X	X	X	X	X	X	X	X	X
Schedule next visit day and time	X	X	X	X	X	X						
Collect all study devices at study end (see device disposition **Table 3** for details)												X
General Questions and Reminders												
Ask if a study subject has general study-related questions and concerns	X	X	X	X	X	X	X	X	X	X	X	X
Ask about the occurrence of adverse events. • Record the event on the appropriate eCRF, if a study subject reports a change in health status that results in a new medical condition or in a deterioration of an existing		X	X	X	X	X	X	X	X	X	X	X

	Run-In Period				Study Period							
	Visit 1 (Office)	Visit 2 (Office)	Visit 3 (Phone)	Visit 4 (Phone)	Visit 5 (Phone)	Visit 6 (Phone)	Visit 7 (Office)					End of Study
							Day 1	Day 2	Day 3	Day 4	Day 5	
Visit Window	**Enrollment /Screening**	**Day -6 (-90 days) Start Run-In**	**Day -3 (-90, +2 days)**	**Day -1 (-1, +2 days)**	**Day 0 (-2, +1 days)**	**Day 6 (-2 days)**	**Day 7 (+10 days)**					
medical condition, such as illness or glycemic problems • Instruct subject to call the investigational center to report any changes to their health status (see adverse event definition).												
Ask subject about device issues		X	X	X	X	X	X	X	X	X	X	X
Remind subject to bring in both study meter and ketone meter at each required office visit.		X				X						
Remind subject to keep their devices charged (Apple Watch, phone, transmitter)		X										
Remind subject have enough insulin pump supplies available		X										
Remind subjects to refer primary healthcare providers to the investigational center staff if they have any questions about study devices and their functions		X										

10.5 Unscheduled Visit

In case an additional visit is performed for study purposes or in case of an early termination visit outside of a normal protocol visit, an unscheduled visit can be used to report data.

Unscheduled visit procedures could include, but are not limited to:

- Insulin pump, CGM and/or app training
- Review adverse event or device deficiency, if any.
- Start of [redacted]

10.6 Early Termination Visit

Whenever possible, the study staff will perform an Early Termination visit when a subject decides to withdraw from the study early or if the subject is withdrawn early upon decision of investigator (during a normal study visit or an unscheduled visit).

Early Termination procedures:

- Review adverse event or device deficiency, if any.
- Collect all study supplies back from subjects.
- Collect questionnaire

10.7 Safety Analysis/Risk Analysis

10.7.1 Glucose Monitoring Risk

- Subjects will be instructed to make sure they have clean fingers when performing fingerstick glucose testing.
- Subjects will have training on diabetes self-management principles.

10.7.2 Hypoglycemic/Hyperglycemic Risk

Intervention and treatment for hypoglycemia and hyperglycemia is addressed in **Section 11.1**.

10.7.3 Calibration of CGM Risk

When an erroneous glucose value is used to calibrate a CGM, the bias is carried through until the next opportunity to calibrate the CGM. This can result in an incorrect bias. Subjects will be trained to appropriate calibration.

10.7.4 Reuse Risk

Durable study devices will be cleaned before each patient use.

10.7.5 Sterilization Risk

The following devices will be supplied sterilized:

- Infusion sets
- Insulin reservoirs
- Sensors

10.7.6 Misuse Risk

Comprehensive training will take place at the initiation visit for investigational center staff regarding the operation of the AHCL, to include all of its functional components and all other study devices to be used during the study at the investigational center.

10.8 End of Study Visit

After the study has been completed (at Visit 7 or in case of early termination), the subjects will complete their end of study visit. The subjects will continue to be treated following the routine practice of each center.

10.9 Glucose and Glycemia Measurements

During the course of the study, the subjects' BG levels and SG levels will be assessed using the methods outlined in this section.

10.9.1 Daily Blood Glucose

Values will be assessed during the study by all subjects using the study meter. The control solution test will be performed following the manufacturer's user guide. Subjects will be trained on the use of the study meter per the manufacturer's instructions.

10.9.2 Sensor Glucose Values

Throughout the study, SG data will be collected using CGM.

10.9.3 AHCL Use

Subjects will be trained to wear the pump and CGM continuously by investigational center staff.

10.9.4 CareLink Uploads

CareLink uploads of the pump will occur automatically via MiniMed Clinical app.

10.10 Subject Questionnaire

A subject questionnaire will be administered at baseline and the end of the study to collect user experience.

10.11 Subject Consent

Informed Consent will be obtained in accordance to ISO 14155:2020.

The investigator or authorized designee must obtain written informed consent from the patient before any clinical study related activity takes place.

In advance of the consent discussion, the patient should receive the EC approved Informed Consent Form (ICF). The process of informed consent shall be documented. Documentation can be sent by mail to the subject (two copies of the ICF will be sent for signature). During the consent discussion the investigator or his/her authorized designee must fully inform the patient of all aspects of the clinical study that are relevant to the patient's decision to participate in the clinical study. Illiterate patients will not be enrolled in this study. All items addressed in the ICF must be explained. The language used shall be as non-technical as possible and must be understandable to the patient and the impartial witness, where applicable.

The patient must have ample time and opportunity to read and understand the ICF to inquire about details of the clinical study, and to decide whether or not to participate in the clinical study. All questions about the clinical study should be answered to the satisfaction of the patient.

Neither the investigator, nor the investigation site staff shall coerce or unduly influence a patient to participate or to continue to participate in the clinical study. The informed consent process shall not waive or appear to waive the patient's rights.

A subject's participation in study procedures cannot begin before the consent process has been properly executed. When the patient decides to participate in the clinical study, the ICF must be signed and personally dated by the patient and investigator or authorized designee.

After all persons have signed and dated the ICF, the investigator must provide the patient with a copy of the Patient Information and the signed and dated Informed Consent Form. A subject's participation in study procedures cannot begin before the consent process has been properly executed.

Based on the definition of vulnerable adult in ISO14155:2020, legally incompetent and illiterate persons, or vulnerable populations will not be included in this clinical study.

A patient contact card will be provided to the patient.

10.11.1 Revisions in Patient Information and Informed Consent Form

Medtronic will inform the investigators whenever information becomes available that may be relevant to the subject's confirmed participation in the clinical study. The investigator or his/her authorized designee should inform the subject in a timely manner.

Medtronic will revise the written Patient Information and Informed Consent Form whenever new information becomes available that may be relevant to the subject's confirmed participation in the

clinical study. Study sponsor will send the revised information to the EC and RA (Regulatory Authority), if applicable, for approval. After approval by the EC and RA, if applicable, a copy of this information must be provided to the participating subjects, and the informed consent process as described above needs to be repeated.

10.12 Assessment of Safety

All AE information is collected in this study. See **Section 12** for further information on the collection of AEs and safety information.

10.13 Recording Data

Data will be captured on eCRFs using Oracle Clinical Remote Data Capture (OC- RDC) module. Original eCRFs will not be considered as source data and supporting documentation will be required, except for the Lab eCRFs which will be considered as source data (results directly transferred from the central lab into eCRF.

Electronic device data will be collected from the study pump using CareLink™ Personal For Clinical Research software. The system uses TLS technology, which encrypts all data it stores. Certain data points stored in the downloaded information may also be captured on the appropriate eCRF.

The investigator will ensure that all eCRFs are completed promptly, completely, and accurately. In the event of data discrepancies, investigational centers will be asked to resolve queries electronically in the OC-RDC system; otherwise, irresolvable data-related issues will be routed to the sponsor for review and final disposition. An audit trail is maintained in OC-RDC to capture any corrections or changes of the eCRFs. System backups for data stored in the Oracle Clinical system will be consistent with Medtronic Standard Operating Procedures (SOPs).

Medtronic will only consider eCRFs to be complete when all discrepancies between source data and eCRF have been resolved. eCRF content will be reviewed by a study monitor, as described in the Monitoring Plan. In addition, specific eCRFs must also be reviewed and electronically signed by the investigator, indicating his/her agreement with the accuracy of all recorded data. It is expected that the investigator and his/her staff will cooperate with the monitoring team and provide any missing data in a timely manner.

10.14 Deviation Handling

A deviation is any instance(s) of failure to follow, intentionally or unintentionally, the requirements of the CIP or the CTA. It is expected that the investigator will conduct this clinical trial in compliance with the CIP and all applicable regulations governing the conduct of clinical research involving human subjects. Deviations will not be issued for the following situations:

- If subjects do not follow the fingerstick recommendations or upload devices unless the site staff did not train the subject on SMBG study procedures or upload procedures.
- If subjects miss or delay protocol visits unless the investigational center staff did not plan the visit according to the protocol schedule.
- If subject did not (fully or partly) complete the Diary.

It is otherwise prohibited to use waivers from the CIP.

10.14.1 Request for Approval of Study Deviations

The investigator shall obtain documented approval from Medtronic, before implementation, for any change in- or deviation from the Clinical Investigation Plan (CIP). In case of study deviations that can affect the subject's rights, safety and well-being or the scientific integrity of the clinical study, approval from the EC and regulatory authority must also be obtained before implementation. The investigator shall timely contact the Clinical Study Manager for review of the proposed change/deviation.

Prior approval is not always realistic in situations where unforeseen circumstances are beyond the investigator's control. However, also in these cases, the event is considered a deviation, and shall be reported.

In any emergency situation the investigator shall exercise his/her judgment to safeguard the subject's interest. Such deviations from the CIP do not require the prior approval of Medtronic. The investigator shall report the deviation as soon as possible to Medtronic and the reviewing EC, if applicable. Medtronic will inform EC and/or RA, if required.

10.14.2 Reporting Requirements for Study Deviations

All study deviations must be recorded on the eCRF regardless of whether medically justifiable, an inadvertent occurrence or taken to protect the subject in an emergency. The date, description and reason for each deviation will be documented.

Investigator must report deviations to Medtronic as soon as possible upon the center becoming aware of the deviation, especially in the following examples of deviations that could impact subject safety, affect the integrity of study data and/or affect subject's willingness to participate in the study:

- Failure to obtain informed consent, i.e., there is no documentation of informed consent
- Informed consent obtained after initiation of study procedures
- Enrollment of a subject who did not meet all inclusion/exclusion criteria
- Performing study procedure not approved by the EC and RA

For medically justifiable conditions that pre-empt a subject's ability to complete a study-required procedure, it may be permitted to report only one deviation that will apply to all visits going forward. This may also apply to other unforeseen situations (e.g. the subject permanently refuses to complete a study required procedure and the data will not contribute to the primary endpoint analysis). However, prior approval from sponsor is required for such situations.

Reporting of deviations by investigator and Medtronic must comply with EC policies, local laws, and/or regulatory authorities' requirements, as applicable.

10.14.3 Analyzing Deviations

Medtronic is responsible for reviewing and analyzing deviations, assessing their significance, and identifying if any additional corrective and/or preventive actions (e.g. amend the CIP, conduct additional training, terminate the investigation) are needed. Repetitive or serious investigator compliance issues may result in initiation of a corrective action plan with the Investigator and investigational center, and in some cases necessitate suspending enrollment until the problem is resolved or ultimately terminating the investigator's participation in the study.

10.15 Subject Exit, Withdrawal or Discontinuation

Subjects may choose to withdraw from the study at any time by notifying investigational center staff of their intent. Whenever possible, the investigational center staff will perform an Early Termination visit when a subject decides to withdraw from the study early or if the subject is withdrawn early upon decision of investigator (during a normal study visit or an unscheduled visit) (described in **Section 10.6**).

Subjects may also be withdrawn from the study at the discretion of the investigator. If a subject chooses to end his or her study participation or if the subject is removed from the study at the investigator's discretion or for failure to meet the study requirements, the reason for withdrawal must be documented both in source documents and on the End of Study eCRF. All study devices and supplies must be returned (as applicable) and documented in the appropriate eCRF.

After subject ends his participation, he will continue to be treated according to routine practice.

10.15.1 Lost to Follow-Up

If a subject does not return to the investigational center for required follow-up visit(s) and cannot be reached, the investigation center personnel should make 3 documented attempts to contact the subject by phone to verify if the subject should be considered "lost to follow-up" - and only if those 3 attempts are unsuccessful, will the patient be considered lost to follow-up. In the event the subject is not able to perform follow-up visits at the investigation center, subject will be considered "lost to follow-up" and this needs to be documented in the End of Study eCRF. All efforts will be made by investigation center personnel to collect all study devices and supplies back from subject, if applicable.

11. Risks and Benefits

11.1 Potential Risks

The potential risks and mitigations associated with the devices used during this study are listed in **Table 5**. Risks associated with the commercially available devices and other products used in the study are listed in the associated device labelling/user guides/instructions for use or investigator brochure.

Table 5. Risks, Prevention and Mitigation

Risks with Infusion Sets	Prevention and Mitigation
Risks with infusion sets may include: • Localized infection • Skin irritation/redness • Bruising • Discomfort/pain • Bleeding • Irritation • Rash • Hyperglycemia secondary to infusion set occlusion or infusion site failure including DKA • Hyperglycemia secondary to site falling off including DKA • Anxiety associated with insertion	Prevention and mitigation include: • Follow the provided user guides for insertions and care of infusion sets. • If an infusion site becomes irritated or inflamed, the infusion set will be removed and another placed in a new location. • In case of hyperglycemia secondary to infusion set occlusion, remove current infusion set and replace with new infusion set and give correction insulin if needed with syringe. • Follow the provided user guides for insulin pump management. • Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems.
Risks with Insulin Administration and Pumps	**Prevention and Mitigation**
Risks with the use of an insulin infusion pump may include the risk of malfunction of the components of the system (pump, software, infusion set and reservoir) as well as the risk of use error during use of the system. Device deficiencies or use errors can result in administration of too much or too little insulin which can lead to the following clinical consequences: • Hypoglycemia • Hyperglycemia • Diabetic ketoacidosis • Severe hypoglycemia with or without associated seizure, coma or death • Kinked cannula leading to hyperglycemia • Infusion set disconnection from pump leading to hyperglycemia • Subject removes the reservoir from the pump but forgets to disconnect the infusion set from the body which results in hypoglycemia or severe hypoglycemia • Dislodged cannula leading to hyperglycemia • A pump error may lead to under delivery or over-delivery of insulin • Battery failure – no insulin delivered	Prevention and mitigation include: • Follow the provided user guides & instructions for insulin pump management which includes information on infusion set change. • Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems. • Instruct to check their meter glucose if their high or low symptoms do not match their sensor alerts or sensor glucose readings in order to make diabetes treatment decisions. • Instruct to have glucose on hand for hypoglycemia. • Instruct to change infusion set if suspected catheter occlusion or administer insulin with syringe for persistent hyperglycemia especially if ketones develop. • During the in-clinic portion of study period, subjects will be under constant surveillance by investigational center staff

• Insulin deterioration leading to hyperglycemia • Incomplete priming; fails to prime tubing and/or cannula, leading to hyperglycemia • Remove a reservoir, without suspending and reconnecting after a while resulting in a hypoglycemia • Patient not filling pump reservoir when needed leading to hyperglycemia • Magnetic resonance imaging resulting in pump transmitter malfunction • Inaccurate insulin delivery due to sudden altitude changes. • Hypoglycemia or hyperglycemia from manual bolus • Hypoglycemia or hyperglycemia from the use of the AHCL Auto Mode feature where sensor glucose values may be used to calculate insulin bolus amounts • Hypoglycemia or hyperglycemia from computer hacking	
Risks with hyperglycemia may include • Diabetic ketoacidosis • Symptomatic ketosis • Cardiovascular event • Dehydration • Potassium and sodium imbalance • Shock • Altered mental status • Coma • Acidosis	Prevention and mitigation include: • Follow the provided user guides for insulin pump management. • Parent(s)/guardian(s)/companion(s) will be present at night with subjects and will be trained on study device and diabetes management principles and instructed to call investigator with problems. • Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems. • Instruct to check their meter glucose if their high symptoms do not match their sensor alerts or sensor glucose readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the sensor glucose value is not accurate. • Alternative method of managing glucose levels will be available (insulin and syringe for example). • During the in-clinic portion of study period, subjects will be under constant surveillance by investigational center staff

Risks with hypoglycemia may include: • Seizure • Coma • Altered mental status • Loss of consciousness • Cardiovascular event • Death • Risk of rebound hyperglycemia with ketosis	Prevention and mitigation include: • Follow the provided user guides for insulin pump management. • Parent(s)/guardian(s)/companion(s) will be present at night with subjects and will be trained on study device and diabetes management principles and instructed to call investigator with problems. • Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems. • Instruct to check their meter glucose if their low symptoms do not match their sensor alerts or sensor glucose readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the sensor glucose value is not accurate). • Instruct to have glucose on hand for hypoglycemia. • During the in-clinic portion of study period, subjects will be under constant surveillance by investigational center staff
Risk with Sensors	**Prevention and Mitigation**
Risks with sensors may include: • Skin irritation or reaction to adhesives • Bruising • Discomfort • Redness • Bleeding • Excessive bleeding due to anticoagulants • Pain • Rash • Infection • Irritation from tapes used with glucose-sensing products • Raised bump • Appearance of a small “freckle-like” dot where needle was inserted • Allergic reaction • Syncopal episode secondary to needle insertion • Soreness or tenderness • Swelling at insertion site • Sensor fracture, breakage or damage • Minimal blood splatter associated with	Prevention and mitigation include: • Follow the provided user guides for insertions and care of sensors. • If a sensor site becomes infected or inflamed, the sensor will be removed and another placed in a new location • Instruct to check their meter glucose if their high or low symptoms do not match their sensor alerts or sensor glucose readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the sensor glucose value is not accurate. • Instruct if there are no sensor values, no treatment decisions will be made until a BG is confirmed.

sensor needle removal • Residual redness associated with adhesive and/ or tapes • Scarring • Scab • Blister • Itchiness • Inflammation • Anxiety • Incorrect sensor glucose reading results in incorrect diabetes management • Subject over-treating secondary to alarms which can result in hyperglycemia or hypoglycemia • Anxiety associated with insertion	
Risks with Transmitter	**Prevention and Mitigation**
Risks with transmitter may include: • Skin irritation or reaction to adhesives • Bruising • Discomfort • Redness • Pain • Rash • Infection • Irritation from tapes used with glucose-sensing products • Raised bump • Allergic reaction • Soreness or tenderness • Residual redness associated with adhesive and/ or tapes • Scarring • Scab • Blister • Itchiness • Inflammation	Prevention and mitigation include: • Follow the provided user guides. • Train on the proper use of the transmitters.
Risks with Serter	**Prevention and Mitigation**
Risks with serters may include: • Improper insertion may lead to device performance issue or hyperglycemia	Prevention and mitigation include: • Follow the provided user guides for insertions and care of device. • Train on the proper use of the serter and skin preparation prior to insertion.
Risks with Fingersticks	**Prevention and Mitigation**
Risks with frequent fingerstick testing may include:	Prevention and mitigation include: • Follow the provided user guides for use of the study meter with fingerstick testing.

• Potential risks associated with frequent meter testing of blood glucose and blood ketones include discomfort and ecchymosis at tips of fingers • Potential risks associated with fingerstick testing include discomfort and bruising	• Train on the proper use of the study meter and fingerstick testing.
Risk with Closed Loop Therapy with Meal Gesture Dosing	**Prevention and Mitigation**

The risks associated with using the insulin pump in closed loop mode with meal gesture dosing are related to the potential for delivery of too much or too little insulin which can result in:
• Hypoglycemia
• Severe hypoglycemia
• Hyperglycemia
• Diabetic ketoacidosis
• User entry error
  ○ Patient entering false glucose values for any reason leading to hypoglycemia and hyperglycemia
  ○ Patient entering false BG values for calibration leading to hypoglycemia or hyperglycemia
• Sensor failure resulting from patient failure to calibrate leading to hypoglycemia or hyperglycemia
• Sensor over-reading resulting in hypoglycemia
• Sensor under-reading resulting in hyperglycemia
• Sensor missed transmission, or any other fault resulting in no SG value, leading to hyperglycemia or hypoglycemia
• Voluntary insulin delivery (with the pump or with a syringe) immediately prior to entering Auto Mode may result in severe hypoglycemia despite shutting down insulin delivery by the algorithm
• Hypoglycemia related to patient taking insulin via injection while in Closed Loop (Auto Mode)
• Hypoglycemia or hyperglycemia related to entering or exiting Closed Loop (Auto Mode)
• Insulin over-delivery due to potential interference from acetaminophen
• Cyber security hacking into pump
	Prevention and mitigation include:
	• Closed Loop Therapy with meal gesture dosing will only be active during the in-clinic portion of study period. Subjects will be under constant surveillance by investigational center staff.
	• Follow the provided user guides for insulin pump management.
	• Train prior to study device use on appropriate device use and diabetes management principles and told to call with problems and instruct to call investigator with problems.
	• Instruct to check their meter glucose if their high or low symptoms do not match their sensor alerts or sensor glucose readings in order to make diabetes treatment decisions.
	• Instruct to check their meter glucose if there are any concerns that the sensor glucose value is not accurate.
	• Instruct if there are no sensor values, no treatments decision will be made until a BG is confirmed.
	• Instruct to have glucose on hand for hypoglycemia.
	• Instruct to avoid the use of products containing acetaminophen
	• If acetaminophen is taken, subjects will be instructed to use additional BG meter readings (they are not to calibrate with those readings) to verify their glucose levels.
	• If acetaminophen is taken, subjects will turn off Auto Correction and exit Auto Mode
	• Pump has cybersecurity encryptions to prevent hacking.
	• Instruct subjects to keep their own insulin pump supplies in a safe place and to have back up supplies in the event they are asked to revert back to their own therapy during the study

	• During the in-clinic portion of study period, subjects will be under constant surveillance by investigational center staff
Risks with hyperglycemia may include: • Diabetic ketoacidosis • Symptomatic ketosis • Cardiovascular event • Dehydration • Potassium and sodium imbalance • Shock • Altered mental status • Coma • Acidosis	Prevention and mitigation include: • Closed Loop Therapy with meal gesture dosing will only be active during the in-clinic portion of study period. Subjects will be under constant surveillance by investigational center staff. • Follow the provided user guides for insulin pump management. • Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems. • Instruct to check their meter glucose if their high symptoms do not match their sensor alerts or sensor glucose readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the sensor glucose value is not accurate. • Instruct if there are no sensor values, no treatments decision will be made until a BG is confirmed.
Risks with hypoglycemia may include: • Seizure • Coma • Altered mental status • Loss of consciousness • Cardiovascular event • Death • Risk of rebound hyperglycemia with ketosis	Prevention and mitigation include: • Closed Loop Therapy with meal gesture dosing will only be active during the in-clinic portion of study period. Subjects will be under constant surveillance by investigational center staff. • Follow the provided user guides for insulin pump management. • Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems. • Instruct to check their meter glucose if their low symptoms do not match their sensor alerts or sensor glucose readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the sensor glucose value is not accurate.

	• Instruct if there are no sensor values, no treatment decisions will be made until a BG is confirmed • Instruct to have glucose on hand for hypoglycemia
Risk with Acetaminophen Use	**Prevention and Mitigation**
Potential risks with acetaminophen may include: • False elevation of sensor glucose readings. The level of inaccuracy depends on the amount of acetaminophen active in subject's body and may be different for each subject • Liver damage, liver failure and/or rare but fatal liver failure can occur • Skin rash and/or serious and potentially fatal skin reactions have been reported • Allergic reactions including those which are serious and potentially fatal can occur • Kidney disease • Lowered blood counts (red cells, and white cells)	Prevention and mitigation include: • Follow the user guide • Instruct to avoid the use of products containing acetaminophen • If acetaminophen is taken, subjects will be instructed to use additional BG meter readings (they are not to calibrate with those readings) to verify their glucose levels • If acetaminophen is taken while the SmartGuard feature is active, subjects will be instructed to use the temp target

11.2 Risk Minimization

Refer to "Prevention and Mitigation" column in the table under **Section 11.1.**

11.3 Potential Benefits

Subjects are not expected to benefit from participation in this study; however, they may gain increased awareness of emerging technologies for diabetes management as a result of their participation.

11.4 Risk-Benefit Rationale

Access to automated insulin devices during the trial may offer improved glycemic control for participants, and may increase understanding of the disorder, due to the fact that the participants will be followed with higher frequency of visits, which will allow a closer medical follow-up when compared to standard of care.

Furthermore, with any externally worn device there are small risks of insulin infusion site reactions, infection, and skin reactions to tapes – however it should be noted that this is no different to standard of care insulin pump therapy and utilizing continuous glucose monitoring.

In addition, any potential risks with this study are minimized by selecting qualified investigators experienced with insulin pump therapy, careful assessment of each subject during the study conduct to effectively monitor and rapidly remedy the problem. Furthermore, subjects can call the site to obtain technical support, if needed.

Medtronic has further minimized the possibility of risks by completing product testing prior to the use of the system in this clinical study, implementing quality control measures into production processes, providing guidelines for subject selection and evaluation, and providing adequate instructions and labelling according to local requirements.

All above these risks are contained within the patient information sheet, and indications and contraindications are provided in the Instructions for Use given to all patients.

12. Adverse Events and Device Deficiencies

Throughout the course of the study, investigational centers will make all efforts to remain alert to possible reportable adverse events (AEs) or untoward findings. The study personnel will elicit reports of adverse events (AEs) from the subject at each visit (including phone calls) starting at the time of signing the informed consent documenting the medical diagnosis, date of event start and end, causality (relationship to device or procedure), treatment, outcome, and description that includes the details of the event.

12.1 Definitions and Classifications of Adverse Events and Device Deficiencies

Medtronic uses the definitions provided in ISO 14155:2020 for AE definitions. Where the definition indicates “device”, it refers to any device used in the study. This might be the device under investigation, or any market released component of the system.

Severe Hypoglycemia is an event requiring assistance of another person due to altered consciousness to actively administer carbohydrate, glucagon, or other resuscitative actions[1]. This means that the subject was impaired cognitively to the point that he/she was unable to treat himself or herself, was unable to verbalize his or her needs, and was incoherent, disoriented and/or combative.

These episodes may be associated with sufficient neuroglycopenia to induce seizure or coma. Plasma glucose measurements may not be available during such an event, but 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.

Severe Hyperglycemia is defined as hyperglycemia (blood glucose greater than (>) 300 mg/dL or 16.7 mmol/L) with blood glucose ketones greater than (>) 1.5 mmol/L, and/or accompanied by symptoms of nausea, vomiting or abdominal pain.

The meter and ketone test strips are supplied for the evaluation of ketone monitoring. Only blood ketones will be recognized (not urine ketones) for assisting in diagnosis of severe hyperglycemia. The monitors/test strips are quality controlled prior to dispensing to subjects. Blood ketones provide contemporaneous understanding of ketone levels associated with elevations in glucose.

Diabetic Ketoacidosis/DKA diagnostic criteria: blood glucose greater than (>) 250 mg/dL or greater than (>) 13.9 mmol/L, arterial pH less than (<) 7.3, bicarbonate less than (<) 15 mEq/L, moderate ketonuria or ketonemia and requiring treatment within a health care facility[2].

Hyperglycemic events will be recorded as DKA if the event includes the presence of all of the following:

- Arterial blood pH less than (<) 7.30 or serum bicarbonate less than (<) 15 mEq/L
- Blood glucose greater than (>) 250 mg/dL or greater than (>) 13.9 mmol/L
- Serum ketones or large/moderate urine ketones
- Symptoms such as polyuria, polydipsia, nausea, or vomiting
- Treatment provided in a health care facility

Adverse Event (AE) (ISO 14155:2020)

Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated.

Note 1 to entry: This definition includes events related to the investigational medical device or the comparator.

Note 2 to entry: This definition includes events related to the procedures involved.

Note 3 to entry: For users or other persons, this definition is restricted to events related to the use of investigational medical devices or comparators.

Adverse Device Effect (ADE) (ISO 14155:2020)

Adverse event related to the use of an investigational medical device.

Note 1 to entry: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

Note 2 to entry: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

Note 3 to entry: This includes 'comparator' if the comparator is a medical device.

Serious Adverse Event (SAE) (ISO 14155:2020)

Adverse event that led to any of the following

a) death,

b) serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:
   1. a life-threatening illness or injury, or
   2. a permanent impairment of a body structure or a body function including chronic diseases, or
   3. in-patient or prolonged hospitalization, or
   4. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
c) fetal distress, fetal death or a congenital abnormality or birth defect including physical or mental impairment

Note 1 to entry: Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

Serious Adverse Device Effect (SADE) (ISO 14155:2020)
Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event

Unanticipated Serious Adverse Device Effect (USADE) (ISO 14155:2020)
Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment.

Note 1: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.

Serious Health Threat (ISO 14155:2020)
Signal from any adverse event or device deficiency that indicates an imminent risk of death or a serious deterioration in the health in subjects, users or other persons, and that requires prompt remedial action for other subjects, users or other persons

Note 1 to entry: This would include events that are of significant and unexpected nature such that they become alarming as a potential serious health hazard or possibility of multiple deaths occurring at short intervals.

Device Deficiency (ISO 14155:2020)

A device deficiency is any inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance.

Note 1: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer including labelling.

Note 2: This definition includes device deficiencies related to the investigational medical device or the comparator.

12.2 Reporting of Adverse Events and Device Deficiencies

The investigator or designee will record all AEs and DDs while the subject is enrolled in the clinical study.

Each AE needs to be assessed for its device or procedure relatedness. A device related AE is associated with the use of the study device (e.g. infection of sensor site or infusion set occlusion resulting in DKA). A procedure related AE is associated with testing related to the study procedures specified in the CIP.

Examples of device or procedure related AEs include:

- ***Device*** related: insertion site infection
- Serious adverse ***device effect***: cellulitis at device insertion site requiring hospitalization
- ***Procedure*** related AE: meal challenge procedure

Subjects participating in the study have diabetes and are expected to experience hypoglycemia and or hyperglycemia. These normal events are not expected to be reported to sponsor on an AE eCRF as this is not considered an untoward event, but rather an expected occurrence. Any glycemic excursion that meets the protocol definition of Severe Hypoglycemia, Severe Hyperglycemia or DKA is considered an untoward event and a worsening from the subject's baseline and would be reported to sponsor on an AE eCRF.

Baseline medical conditions should only be reported to sponsor on an AE eCRF, if there is a worsening from the subject's baseline. For example, a subject previously diagnosed with Asthma is hospitalized for severe asthma attack would be a reportable event.

Adverse events will be documented in the subject source file and reported to sponsor on an eCRF. The investigational center is responsible for documentation of AEs including obtaining source documents related to the event, such as emergency medical technician/paramedic reports, hospital records (admission summary; lab results, test results, discharge summary) or device uploads to support the event. Source documents will be reviewed to determine if additional AEs have occurred and require reporting.

Adverse events that have not resolved at the time of the subject's discontinuation or completion of the study should have an "outcome" of Not Recovered/Not Resolved at study end in subject source and on an eCRF. The investigator should ensure that subject is aware of any follow-up or additional treatment that is required for any ongoing AE at end of study participation; however, there will be no eCRF entry for the ongoing follow-up.

Table 6. Adverse Event and Device Deficiency Reporting Requirements by Investigator

Event Type to Report	Timeframe for Reporting to Medtronic	Reporting to Regulatory Authority and Ethics Committee
▪ Serious Adverse Device Effect (SADE) ▪ Unanticipated Serious Adverse Device Effect (USADE) ▪ Serious Adverse Event (SAE) ▪ Device Deficiency that might have led to a SADE	Report immediately, but **no later than 24 hours** after investigational center study personnel's first awareness of the event (or sooner if required by local regulation)	Submit per local reporting requirements
▪ Adverse Event (AE) ▪ Adverse Device Effect (ADE) ▪ Device Deficiency (DD)	Report in a timely manner from the investigator's / investigational center first knowledge of the event	Submit per local reporting requirements

Medtronic is obligated to report adverse events and device deficiencies that occur during this study to the regulatory authorities and EC as per local requirements.

Adverse Event and Device Deficiency Classification

All AE and DD will be reviewed by a Medtronic representative. AEs will be classified according to the responsibilities and definitions provided in **Table 7** and **Section 12.4**.

Upon receipt of AE/DD at Medtronic, a Medtronic representative will review the AE/DD for completeness and accuracy and when necessary will request clarification and/or additional information from the Investigator. Medtronic will utilize MedDRA for Regulatory Activities, to assign a MedDRA term for each AE based on the information provided by the investigator.

Regulatory reporting of AEs and DDs will be completed according to local regulatory requirements. Refer to **Table 6** for a list of required investigator and Medtronic reporting requirements and timeframes. It is the responsibility of both to abide by any additional AE reporting requirements stipulated by the EC responsible for oversight of the study.

Table 7. Adverse Event Classification Responsibilities

What is classified?	Who classifies?	Classification Parameters
Relatedness	Investigator	Device, Procedure
	Sponsor	Device, Procedure
Seriousness	Investigator	SAE, DD with SADE potential
	Sponsor	SAE, USADE, DD with SADE potential

What is classified?	Who classifies?	Classification Parameters
Diagnosis	Investigator	Based on presenting signs and symptoms and other supporting data
	Sponsor	MedDRA term assigned based on the data provided by Investigator

12.3 Notification of Adverse Events and Device Deficiencies

Sponsor Notification:

The investigational center staff must report all reportable AEs and DDs to Medtronic in a timely manner. All Severe Hypoglycemia, DKAs, USADEs, DDs with SADE potential, SAEs, and SADEs should be reported as soon as possible (desired within 24 hours of investigator or study coordinator awareness) to Medtronic. For the previously mentioned events, the AE eCRF will be completed with all known details as soon as possible, this will serve as notification to Medtronic.

If the study database cannot be accessed due to technical problems, contact the sponsor via email at dl.diabetesclinicalresearchsafety@medtronic.com and provide the known details of the event. Do not include any patient-identifiable information in the e-mail. Once the access issue has been corrected, the event should be entered onto an AE eCRF.

Source documents that support the event (e.g., clinic notes, hospital admission and discharge records, lab reports, EMT reports, ER/Urgent Care) should be provided to the sponsor via the Medtronic BOX safety folder. All source documents/medical records should be redacted of personal information (full name, address, etc.) prior to providing to the sponsor. Each source page should be identified with the subject ID.

12.4 Causality Assessment

An AE is not automatically related to the study device or procedure simply because the subject is wearing the device and participating in the study. The event should be reviewed to determine if the device or study procedure could have possibly caused the event and therefore is related to the study device or procedure.

Causality assessment is the determination of the relationship between an AE and the device being studied. It is expected that the investigational center will review all elements surrounding the AE to properly assess the causality of the event to the study device or to a study procedure.

Investigators should classify the relationship between the AE and the study device or study procedures using one of the four possible causality categories listed below:

1) Not related: relationship to the device, comparator or procedures can be excluded when:

- The event has no temporal relationship with the use of the investigational device or the procedures related to the application of the investigational device
- The event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
- The discontinuation of medical device application or the reduction of the level of activation/exposure – when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the event;
- The event involves a body-site, or an organ not expected to be affected by the device or procedure;
- The event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);
- The event does not depend on a false result given by the investigational device used for diagnosis[1], when applicable;

In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the event.

2) Possible: the relationship with the use of the investigational device or comparator is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases were relatedness cannot be assessed or no information has been obtained should also be classified as possible.

3) Probable: the relationship with the use of the investigational device or comparator seems relevant and/or the event cannot reasonably be explained by another cause, but additional information may be obtained.

4) Causal relationship: the event is associated with the investigational device, comparator or with procedures beyond reasonable doubt when:

- The event is a known side effect of the product category the device belongs to or of similar devices and procedures;
- The event has a temporal relationship with investigational device use/application or procedures;
- The event involves a body-site or organ that:
  - The investigational device or procedures are applied to;
  - The investigational device or procedures have an effect on;
- The event follows a known response pattern to the medical device (if the response pattern is previously known);

[1] If an investigational device gives an incorrect diagnosis, the patient might, for example, receive an unnecessary treatment and incur all the risks that accompany that treatment, or might be incorrectly diagnosed with a serious disease. In other cases, the patient might not receive an effective treatment (thereby missing out on the benefits that treatment would confer) or might not be diagnosed with the correct disease or condition.

- The discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the event (when clinically feasible);
- other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment) have been adequately ruled out;
- Harm to the subject is due to error in use;
- The event depends on a false result given by the investigational device used for diagnosis, when applicable;

In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the event.

Example: A severe hyperglycemia AE with the following event description would have the following causality assessment for device relatedness:	
Improved glucose without an infusion set/site change	Not related
Changed infusion set with glucose improvement	Possible
Infusion Set Fell Out, Bent Cannula, Occlusion Alarm	Causal Relationship

12.5 Device Deficiencies and Troubleshooting

The investigational center will be consulted for device troubleshooting if assistance is needed by subject to operate study devices and apps. If DD is detected the investigational center staff will complete the appropriate eCRF(s). All Device Deficiencies that did not lead to an Adverse Event should be reported on the Device Deficiency eCRF, one for each Device Deficiency, completing as much information as is available.

Note that device deficiencies that result in an AE to the subject should be captured as an AE CRF only. Each device deficiency will be assessed for SADE potential defined as:

A Device Deficiency that did not lead to an Adverse Event, but could have led to a SADE:

a) if either suitable action had not been taken,
b) if intervention had not been made, or
c) if circumstances had been less fortunate

13. Data Review Committees

13.1 Clinical Events Committee Review

A Clinical Event Committee (CEC) consisting of external (non-Medtronic employed) physicians with an expertise in endocrinology and the management of diabetes, including insulin pumps and CGM will be convened. The CEC will review on periodic basis AEs and may include reports of:

- Serious Adverse Event (SAE)

- Serious Adverse Device Effect (SADE)
- Unanticipated Serious Adverse Device Effect (USADE)
- Severe Hypoglycemia
- Diabetic Ketoacidosis (DKA)
- Deaths

The CEC will assess events to determine agreement or disagreement with the investigator classification of an event.

If the CEC disagrees with the investigator's classification of the event, the rationale will be provided to the investigator. If the investigator agrees with the CEC's adjudication, the CRF documenting the AE will be updated accordingly.

If the investigator does not agree with the CEC's adjudication classification, both determinations will be provided within the final report; however, the CEC's adjudication will be used for data analysis. The disagreement will also be included in reporting to ECs and regulatory authorities, if required.

14. Statistical Design and Methods

14.1 General Aspects of Analysis

All data collected from the time of screening until the end of the study will be collected either on eCRFs and electronically by uploading the various devices. Data and analysis will be summarized in a Clinical Study Report. Any deviations from original statistical plan and the rationale will be described in the Clinical Study Report.

No interim analysis is planned.

14.2 Subject Disposition

The number of subjects enrolled, completed, early terminated the study will be presented. The reasons for discontinuing prior to study completion will be summarized.

14.3 Subject Demographics and Baseline Characteristics

Subject demographics and baseline characteristics will be summarized by descriptive statistics (mean, standard deviation, minimum, median, and maximum) for continuous variables and by counts and percentages for categorical variables.

14.4 Sample Size Considerations

Given that this study is not statistically powered, no sample size calculation was performed. A total of up to 40 subjects will be enrolled at one investigational center in Israel to have at least 16 subjects complete the study. Subjects may repeat participation in the study at the request of the Sponsor and at the discretion of the investigator but will only be counted once toward the total number of subjects.

14.5 Analysis of Endpoints

Analysis will be performed by Klue Health App software release version, if applicable.

14.5.1 Primary Endpoints

- Post-prandial Time in range (% of SG within 70-180 mg/dl) At-Home and In-Clinic Period will be summarized, respectively.

14.5.2 Safety Endpoints

- Number of (S)AEs, (S)ADEs, USADEs, Severe hypoglycemic events, DKA events, and Device Deficiencies

14.5.3 Other Endpoints

All measurements performed by Study Period (At-Home and In-Clinic period).

- Post-prandial Time in different ranges (% of SG): SG <54, 70 mg/dL, SG > 180, 250 mg/dL
- Change in post-prandial % of time in euglycemia (70-180 mg/dL) for meal challenges (intervention versus baseline)
- Change in post-prandial % of time in different ranges (% of SG): SG <54, 70 mg/dL, SG > 180, 250 mg/dL for meal challenges (intervention versus baseline)
- 24 hour Time in range (% of SG within 70-180 mg/dl)
- 24 hour Time in different ranges (% of SG): SG <54, 70 mg/dL, SG > 180, 250 mg/dL
- Number of Events, Area Under Curve (AUC) and Time in the hyperglycemic range: sensor glucose (SG) > 180, 250 mg/dL
- Number of Events, AUC and Time in the hypoglycemic range: SG < 54 and 70 mg/dL
- Time spent in Auto Mode versus time spent in Manual Mode
- Change of Total Daily Dose (TDD) of insulin from baseline to EOS Period
- Change in BG values during meal challenge (BG prior and BG 2 hours after meal)
- Insulin delivery at postprandial: Total unit of insulin in first 15 minutes, 60 minutes, 120 minutes, and 240 minutes postprandial
- Subgroup analysis by type of meals
- Between period analyses of all above (At-Home vs. In-Clinic)

14.5.4 Subject Feedback

- Descriptive summary will be used to characterize study questionnaire

14.6 Handling Missing Data

All available data will be included in the data listings and tabulations. No imputation will be applied for the missing data.

15. Ethics

15.1 Statement(s) of Compliance

This clinical study will be conducted in compliance with the principles originating from the Declaration of Helsinki (2013), the international standard ISO 14155:2020 ('Clinical Investigation of medical devices for human subjects'), laws and regulations of the countries in which the clinical study is conducted, including data protection laws, the Clinical Investigation Agreement and the Clinical Investigation Plan.

The study will also be conducted in compliance with the principles of good clinical practice (GCP) meaning that the study design, conduct, performance, monitoring, auditing, recording, analysis and reporting will assure that the data and results are credible and accurate and that the rights, safety and well-being of subjects are protected. GCP includes review and approval by an independent ethic committee (EC) and Regulatory authority before initiating the investigation, ongoing review of the investigation by an EC and RA and obtaining and documenting the freely given informed consent of the subject before their participation in the investigation.

All principles originating from the Declaration of Helsinki (2013) have been implemented in this clinical study including but not limited to informed consent process, EC and RA approvals, study training, preclinical testing, risk benefit assessment, publication policy.

The sponsor shall avoid improper influence on, or inducement to the subject, monitor, any investigator(s) or other parties participating in, or contributing to, this study.

15.2 EC Approval

This CIP, any subsequent amendments to this CIP, the ICF, subject material, and any form of subject recruitment information (e.g. advertisements), if applicable, relating to this study will be approved by the responsible EC.

The investigational center will not initiate any subject activities until EC approval has been granted, the sponsor has cleared the investigational center to begin the study, and the investigational center staff has been appropriately trained to conduct the study.

If the EC imposes any additional requirements, Medtronic will prepare required documents and send them to the EC.

15.3 Regulatory Submission

In countries where submission to the regulatory authority is required per local law, no patients will be enrolled in the clinical study until the particular regulatory authority has approved the current Clinical

Investigation Plan (and amendments) of the clinical study and other documents as required according to the local requirements.

If the regulatory authority imposes any additional requirements (e.g. safety reports, progress reports etc.), Medtronic will prepare the required documents and send them to the respective authority.

Other documents that are referred to in this CIP will be made available upon request.

15.4 Investigator Responsibilities

This study will be conducted at the investigational centers where all study-related activities will be performed and will be led by a PI. Per ISO14155:2020, an investigator means "individual member of the investigation center designated and supervised by the principal investigator at an investigation site to perform critical clinical-investigation-related procedures or to make important clinical-investigation related decisions."

The investigator's responsibilities include but are not limited to:

- Conduct of the investigation in accordance with the CIP and Clinical Trial Agreement, applicable regulations, and any conditions of approval imposed by the reviewing EC or regulatory authority requirements
- Conduct of investigation in accordance to International guidelines for clinical trials on medical devices ISO 14155:2020
    - To supervise a clinical study in which some study tasks are delegated to employees or colleagues of the investigator or other third parties, and
    - To protect the rights, safety, and welfare of study subjects.
- Protecting the rights, safety, and welfare of subjects under the investigator's care
    - Providing reasonable medical care for study subjects for medical problems that arise during participation in the trial that are, or could be, related to the study intervention
    - Providing reasonable access to needed medical care, either by the investigator or by another identified, qualified individual (e.g., when the investigator is unavailable, when specialized care is needed)
    - Adhering to the CIP so that study subjects are not exposed to unreasonable risks
- Controlling devices under investigation
- Investigator is responsible for providing adequate supervision of those to whom tasks have been delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of a clinical study.
- Ensuring that the requirements for obtaining informed consent are met in accordance with ISO 14155:2020
- Disposing of device properly. Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator shall return to

the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.

- Allowing study devices to be used only with subjects under the investigator's supervision and to supply study devices only to persons authorized to receive it
- Ensuring that investigational center staff are adequately trained to perform their assigned duties
- Maintenance of accurate, complete, and current records relating to the investigator's part of an investigation, to include:
    - all relevant correspondence with another investigator, an EC, the sponsor, a monitor, regulatory authorities, including required reports.
    - records of receipt, use or disposition of study devices
    - records of each subject's case history and exposure to the device
    - the CIP, with documents showing the dates of and reasons for each deviation from the CIP
- Preparation and submission to Medtronic and, when required, regulatory agency and the reviewing EC, the following complete, accurate, and timely reports:
    - any reportable AEs (see **Section 12.3**) occurring during an investigation
    - progress reports on the investigation as required by the regulatory agency and EC
    - any deviation from the CIP made to protect the life or physical well-being of a subject in an emergency any use of the device without obtaining informed consent
    - any further information requested by the regulatory agency and EC about any aspect of the investigation
    - any other records the regulatory agency requires to be maintained by regulations or by specific requirement for a category of investigations or a particular investigation
- Permitting regulatory authorities to inspect and copy any records pertaining to the investigation including, in certain situations, those which identify subjects
- Meeting with the monitor to discuss study progress and findings
- Ensuring that investigational center resources are adequate to fulfill the obligations of the study
- Ensuring completion of eCRF to include entry and addressing discrepancies in a timely fashion and approving selected eCRFs.

Only authorized study personnel as listed on the Delegation of Authority Log are permitted to consent subjects, receive, dispense, dispose of and return investigational products, conduct subject visits, insert devices, and enter data on eCRFs. These tasks may be delegated by the investigator. However, the investigator is ultimately responsible to ensure investigational center-staff are qualified and perform the tasks that have been delegated to them correctly. In addition, the investigator is responsible for the conduct of investigational center in the execution of the clinical trial.

The investigator's signature on the Investigator Statement confirms that the investigator is familiar with the CIP in its entirety and agrees to conduct this study in accordance with the provisions of the CIP and all applicable regulations. The investigator, prior to the initiation of any study related activity, will sign the Investigator Statement. If the sponsor discovers that an investigator is not complying with the

Investigator Agreement, CIP, or other regulatory requirements, the sponsor shall promptly secure compliance or discontinue that investigator's participation in the study.

15.5 Role of the Sponsor's Representatives

Sponsor's representatives may provide support as required for the study including providing study specific training to the investigational center personnel conducting study activities. Sponsor's representatives may also provide technical support under supervision of the PI following routine practice in the participating countries (i.e. pump or CGM training) and for study specific activities (i.e. data uploads, IT support). In the applicable participating investigational centers where sponsor is involved in subject device trainings, the sponsor's representatives providing technical support will be listed on the sponsor technical support list. No data entry on the eCRF shall be performed by Medtronic personnel or their representatives.

16. Study Administration

16.1 Investigator Qualification

The following requirements will be evaluated for each investigator considered for participation in the clinical study:

- Investigator/investigational center is qualified by training, education, and relevant experience appropriate to the
  use of the product and associated procedures (Endocrinology or Diabetology expertise)
- Investigator/investigational center has Medtronic MiniMed 670G or 780G System experience, including CareLink usage
- Investigator/investigational center expects to have adequate time and resources to conduct the study throughout the duration
- Investigator/investigational center has access to an adequate number of eligible subjects
- Investigator/investigational center has past experience in conducting clinical studies
- Investigator/investigational center has interest in participating in pre-market interventional studies with devices
- Investigator/investigational center has the ability to comply with applicable EC and regulatory requirements
- Investigator is not debarred, disqualified, or working under sanctions in applicable regions

16.2 Training of Clinical Staff

In order to conduct the study, investigational center staff must have the appropriate medical training required. Training of the investigational center staff on the conduct of the study and system being studied will be initiated before the CIP is implemented. All participating physicians and coordinators will be familiarized with the system. Other members of the investigational center staff may require training depending on their role listing in the Delegation of Authority Log.

The PI is responsible for ensuring that investigational center staff are trained to perform their assigned duties per the Delegation of Authority Log. Individual investigational center staff must be appropriately trained prior to performing study related tasks.

16.3 Monitoring

Monitoring visits will be conducted at the start, during and at the closure of the clinical study in accordance with Medtronic SOPs and the Monitoring Plan and conducted by a vendor. At minimum, it will be verified whether signed and dated informed consent forms have been obtained from each subject at the point of enrollment and that AEs discussed in **Section 12** were reported via completion of the Adverse Event CRFs. More details regarding the monitoring activities (frequency of monitoring visits, planned extent of source data verification) are described in the Monitoring Plan.

16.3.1 Accessibility of Investigational Center Staff and Study Materials

The principal investigator(s), his/her delegate(s) and the study coordinator(s) shall be accessible to Medtronic field personnel, monitor and the Clinical Study Manager. This accessibility is of particular importance for reviewing data in the electronic Case Report Form (eCRF).

Medtronic clinical representatives or delegates will be granted access by the investigational center to all source documents including electronic source documents, if applicable, for the purposes of monitoring, audit, or inspection. Source data access should be prepared by investigational center staff prior to any visit. If applicable, where copies of the original source document as well as printouts of original electronic source documents are retained, these shall be signed and dated by a member of the investigational center team with a statement that it is a true and complete reproduction of the original source document ("certified copy").

16.3.2 Audits and Investigational Center Inspections

In addition to regular monitoring visits, Medtronic may conduct quality audits at participating investigational centers. The purpose of an audit is to verify the adequate performance of the clinical study related activities independent of the employees involved in the clinical study, verify adherence to external regulations and internal policies and procedures; assess adequacy and effectiveness of clinical policies and procedures; assure compliance with critical study document requirements; confirm integrity and accuracy of clinical study data; and protect the safety, rights and welfare of study subjects.

Regulatory authorities may also perform inspections at participating investigational centers. Any regulatory authority inspection announcements shall be forwarded immediately to the Clinical Study Manager.

The investigator and/or institution shall permit Medtronic and regulatory authorities direct access to source data and documents, taking into account any restrictions due to local law, to perform clinical study related monitoring, audits, EC review, and regulatory inspections.

16.4 Data Management

16.4.1 Electronic Case Report Forms (eCRFs)

The investigator must ensure accuracy, completeness and timeliness of the data reported in the eCRFs and in all other required reports. Data reported on the eCRFs which are derived from source documents, such as subject medical records, must be consistent with the source documents and discrepancies need to be justified in a documented rationale.

Only authorized persons can complete eCRFs. eCRFs shall be signed by investigational center staff as specified on the Delegation of Authority Log included in the Investigator Site Binder. The OC-RDC system maintains an audit trail on entries, changes, and corrections in the eCRFs.

A copy of the eCRFs to be used in this clinical study is available under a separate cover, upon request to the Sponsor and in the Investigator Site File. Investigational centers will be trained in the use of eCRFs. Access to final eCRFs for study conduct will be granted after training is performed and prior to patient's enrollment.

16.4.2 Paper Study Worksheets

All investigational centers will receive paper worksheets upon request, which specify the required data collection in the CRFs, and some additional instructions to ensure correct completion. The study worksheets are a supplement of the patient's hospital/clinic file and completed worksheets will be considered as source documents. Only authorized persons can complete the worksheets as specified on the Delegation of Authority Log included in the Investigator Site File.

16.4.3 Medtronic Carelink System for Clinical

During the course of the study, subject's BG values may be assessed from the Accu-Chek Guide Link study meter. The SG values may be assessed from the study pump. The study pump will be uploaded in Carelink system by the investigator or designated investigational center staff and subjects at home. The system uses TLS technology, which encrypts all data it stores. The data in the different databases are linked to each other via the subject's ID.

16.4.4 Patient Questionnaires

The questionnaires will be provided in local language in the countries. The data will initially be collected on paper questionnaires that will be kept at the investigational center. For more information, please refer to questionnaire instructions.

The investigator, or designated investigational center personnel, will then copy the answers of the subject from the paper questionnaires into the OC-RDC system. It is important that the investigator or designated investigational center personnel verifies the questionnaires for completeness before subject leaves the investigational center.

16.4.5 [redacted]

[redacted]

16.4.6 Time Windows for Completion and Submission of Case Report Forms

It is expected that eCRFs are completed in a timely manner, with the exception of reportable events (see **Table 6**), which need to be recorded immediately after awareness of the investigational center staff on the Adverse Event or Device Deficiency eCRFs. After data entry, eCRFs should be submitted (i.e. saved) so that monitors can proceed with data verification without delay.

16.4.7 Data Review and Processing

Data management will be done according to Medtronic SOPs and the Data Management Plan for this clinical study.

Collected data will be reviewed for completeness, correctness, and consistency, as per the monitoring plan. In case of issues, queries will be entered on the respective eCRF for the investigator to complete, correct, or comment on the data.

16.5 Direct Access to Source Data/Documents

The subject's clinic file, CareLink Personal/CareLink system software data, laboratory reports, survey and source documents are handled as source data.

Medtronic clinical representatives or delegates will be granted access by the investigational center to all source documents including electronic source documents or copies of electronic source documents, if applicable, for the purposes of monitoring, audit, or inspection.

16.6 Confidentiality

The investigator will ensure that the subject's confidentiality maintained. All records and other information about subjects participating in this clinical study will be treated as confidential. Subject confidentiality will be maintained throughout the clinical study to the extent permitted by law. That is, every attempt will be made to remove subject identifiers from clinical study documents. For this purpose, a unique subject identification code (study – investigational center – subject number) will be assigned and used to allow identification of all data reported for each subject. This will also ensure that the information can be tracked back to the source data. All laboratory specimens, evaluation forms, reports, and other records that leave the investigational center will be identified only by the subject ID code in order to maintain subject confidentiality. All records will be kept in a secure environment and all computer entry and networking programs will be done with coded numbers only.

The study monitors and other authorized representatives of the sponsor may inspect all documents and records required to be maintained by the investigator, including but not limited to, medical records. The investigator will inform the subjects that the above-named representatives will review their study-related records without violating the confidentiality of the subjects. Study data may also be made available to third parties, e.g., in the case of an audit or inspection performed by regulatory authorities, provided the data are treated confidentially and that the subject's privacy is guaranteed.

Subjects will not be identified in any publicly released reports of this study.

16.7 Liability and Subject Compensation

The subjects may receive compensation for participation in this study in the form of paid accommodation during the clinic stay. Travel fees to the investigational center may be reimbursed for study specific visits if required by local regulations. Refer to the ICF for details of the subject's compensation.

The Medtronic International Trading Sàrl is a wholly owned subsidiary of Medtronic, which as the parent company of such entity maintains appropriate clinical study liability insurance coverage as required under applicable laws and regulations and will comply with applicable law and custom concerning specific insurance coverage. If required, a Clinical Trial Insurance statement/certificate will be provided to the EC or regulatory authority.

16.8 CIP Amendments

An investigator or study team member can propose any appropriate modification(s) of the Clinical Investigation Plan or investigational device/product or investigational device/product use. Medtronic will review this proposal and decide whether the modification(s) will be implemented.

Medtronic can decide to revise the CIP based on new information and will submit any significant amendment to the CIP, including a justification for this amendment, to the appropriate regulatory authorities for their approval and to the investigators to obtain approval from their EC. The investigator will only implement the amendment after approval from the EC, regulatory authority and sponsor. Administrative amendments to the CIP will be submitted to the EC for notification. Furthermore, the principal investigator shall sign any approved amendment for agreement.

16.9 Investigational Center Compensation

Medtronic contracts with participating institutions/investigators through a Clinical Trial Agreement that defines the scope and responsibilities and associated compensation related to carrying out the obligations under a clinical study sponsored by Medtronic.

16.10 Record Retention

The Principal Investigator will retain all records and documents pertaining to this study in accordance with local law and regulations for a minimum period of 15 years (or longer if local laws require) after market release in his/her region or termination of the study, whichever is longer. In case of investigational center closing with no patients enrolled, the documents shall be obtained by all entities (PI, EC and CA) at the investigational at least 1 year, from the closing of the investigational center. They will be available for inspection by the appropriate regulatory authorities. In addition, the investigator

will retain the source documents from which the information entered on the eCRF was derived. The investigator should take measures to prevent accidental or early destruction of the clinical study related materials and will ensure that essential study documents are not destroyed until written permission has been obtained from Medtronic. Medtronic will retain the study records according to Medtronic policy.

16.10.1 Investigator Records

The investigator is responsible for the preparation and retention of the records cited below. All of the below records, with the exception of case history records and case report forms, should be kept in the Investigator Site File (i.e., the study binder provided to the investigator) or Subject Study Binder. CRFs must be maintained and signed electronically within the electronic data capture system during the study. The following records are subject to inspection and must be retained for a period of two years (or longer as local law or hospital administration requires) after product approval or the date on which the investigation is terminated.

- All correspondence between the EC, sponsor, monitor, RA and the investigator that pertains to the investigation, including required reports.
- Subject's case history records, including:
  - Signed and dated ICF signed by subject and investigator.
  - Observations of AEs/ADEs/DDs
  - Medical history
  - Follow-up data
  - Documentation of the dates and rationale for any deviation from the protocol
- List of investigational centers
- FD (if applicable)
- Subject screening log & SID log
- Lab certificate
- Device Disposition Logs containing Model and serial/lot numbers, subject IDs of the subjects receiving device, receive and return date by patient, returned-to-sponsor dates, disposal /destruction date, initials of all persons who received device from sponsor or subject, returned or disposed/destruct device, and reason and method of disposal/destruction.
- All approved versions of the CIP and ICF
- Signed and dated CTA.
- CV signed and dated of principal investigators
- Documentation of delegated tasks
- EC approval documentation. Written information that the investigator or other study staff, when member of the EC, did not participate in the approval process. Approval documentation must include the Ecs composition, where required per local law.
- RA notification, correspondence and approval, where required per local law.

- Study training records for investigational center staff.
- Insurance certificates
- Final Study Report including the statistical analysis.

16.10.2 Sponsor Records

Medtronic shall maintain the following accurate, complete, and current records:

- All correspondence which pertains to the investigation
- Investigational device traceability record containing Model and serial numbers of devices, shipping date and name and address of person that received shipped device, location (if different than person shipped to), transfer and receipt by Medtronic dates.
- Signed Investigator Trial Agreements, FD (if applicable) and current signed and dated (Europe only) CV of principal investigator and key members of the investigational center team (as required by local law), delegated task list
- All approved IC templates, and other information provided to the subjects and advertisements, including translations
- Copies of all EC approval letters and relevant EC correspondence and EC voting list/roster/letter of assurance
- Names of the institutions in which the study will be conducted
- RA correspondence, notification and approval as required by national legislation
- Insurance certificates
- Names/contact addresses of monitors
- Monitoring visit reports
- Statistical analyses and underlying supporting data
- Final report of the study
- The CIP, IB/Report of Prior Investigations summary and study related reports, and revisions
- Study training records for investigational center personnel and Medtronic personnel involved in the study
- Any other records that local regulatory agencies require to be maintained.

Medtronic records and reports will be maintained in a password-protected document management system, and paper documents (where applicable) will be stored in stored in secured file cabinets at Medtronic during the course of this study.

After closure of the study Medtronic will archive records and reports indefinitely.

16.11 Reporting Requirements

16.11.1 Sponsor Reports

Medtronic shall prepare and submit the following complete, accurate, and timely reports listed in the tables below (by geography). In addition to the reports listed below, Medtronic shall, upon request of the reviewing EC or RA, provide accurate, complete and current information about any aspect of the investigation. Safety data Medtronic reporting requirements are listed in **Section 12.**

Table 8. Sponsor Reports

Report	Submit to	Description/Constraints
Premature termination or suspension of the clinical investigation	Investigators, EC, RAs and Head of the Institution	Provide prompt notification of termination or suspension and reason(s). (ISO 14155:2020)
Withdrawal of EC approval	Investigators, Head of Institution, EC and RAs	Investigators, ECs will be notified only if required by local laws or by the EC.
Withdrawal of CA approval	Investigators, Head of Institution, EC, and RAs	Investigators, ECs will be notified only if required by local laws or by the EC.
Final report	Investigators, EC, and RAs if required	• The investigator shall have the opportunity to review and comment on the final report. • If a clinical investigator does not agree with the final report, his/her comments shall be communicated to the other investigator(s). • The coordinating investigator shall sign the report. If no coordinating investigator is appointed, then the signature of the principal Investigator in each study site should be obtained. (ISO 14155:2020)
Study deviation	Investigators and RAs, if required	Ensure that all deviations from the CIP are reviewed with the appropriate clinical investigator(s), are reported on the CRFs and the final report of the clinical investigation. (ISO 14155:2020) Study site specific study deviations will be submitted to investigators periodically.

16.12 Suspension or Early Termination

16.12.1 Early Study Suspension or Termination

Sponsor or Regulatory Authority may decide to suspend or prematurely terminate the clinical study (e.g. if information becomes available that the risk to study subject is higher than initially indicated, lack of enrollment, if interim analysis indicates that the results significantly differ from expectations relative to study objectives or statistical endpoints, or because of a business decision). If the clinical study is terminated prematurely or suspended, Medtronic shall promptly notify the Regulatory Authority and inform the investigators of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform the reviewing EC and the study subjects, as applicable by local laws and regulations.

16.12.2 Early Investigational Center Termination or Suspension

Sponsor, EC or a Regulatory Authority may decide to suspend or prematurely terminate an investigational center (e.g. in case of non-compliance to the CIP, lack of enrollment). If an investigational center is suspended or prematurely terminated, sponsor shall promptly inform the investigator(s) and the Regulatory Authority of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform the reviewing EC and the study subjects, as applicable by local laws and regulations.

When the risks are found to outweigh the potential benefits or when there is conclusive proof of definite outcomes, investigators must assess whether to continue, modify, or immediately stop the clinical study in the respective investigational center and immediately inform the sponsor and EC, if applicable.

16.12.3 Subject Follow-Up In Case of Termination

In case of early investigational center suspension or termination, all subjects should be called to plan an Early Termination visit (described in **Section 10.8**) at the investigational center. All efforts will be made to complete and report all study observations at the time of termination. The subject will return the study devices to the investigational center.

16.13 Study Closeout

At the time of a study close-out, the investigators will be notified by the sponsor. Appropriate notification and final study report will be provided to EC and Regulatory Authority, if required per local laws and regulations.

16.14 Publication and Use of Information

The contents of this CIP, documentation, and results pertaining to this study are confidential and may not be published or disclosed without the written consent of Medtronic. Publications and presentations referring to this clinical study will be coordinated by Medtronic to allow the use of all available data.

The identity of the subjects may not be disclosed, unless required by law, to any persons not immediately involved in the study or the study procedures. The study will be publicly registered on http://www.clinicaltrials.gov and https://my.health.gov.il prior to subject enrollment.

17. References

1. Cryer PE. Defining and reporting hypoglycemia in diabetes: A report from the American diabetes association workgroup on hypoglycemia. Diabetes Care 2005;28:1245-9.
2. Hyperglycemic Crises in Diabetes. Diabetes Care 2004;27:S94-S102.
3. EMEA. Clinical Safety Data Management: Definitions and Standards for Expedited Reporting. ICH Topic E2A 2006.

18. Appendices

18.1 Names and Addresses

18.1.1 Investigational Centers Information

The names and addresses of investigators and participating investigational centers will be kept under separate cover. This list will be provided to the participating investigators and sponsor shall inform the investigators in case changes occur in the list of participating investigational center. The most current list is available upon request.

18.1.2 Monitors Contact Information

The names and addresses of monitors will be kept under separate cover. This list will be provided to the participating investigators and sponsor shall inform the investigators in case changes occur in the list. The most current list is available upon request.

18.1.3 Sponsors Contact Information

The names and addresses of sponsor team will be kept under separate cover. The most current list of the contact persons is available upon request.

18.1.4 Vendors Contact Information

The names and addresses of vendors providing services for the study will be kept under separate cover. The most current list of the contact persons is available upon request.

18.2 Labelling and IFUs of Devices

The current labelling and IFU for the study devices will be provided to the investigators under a separate cover.

18.3 Sample Informed Consent Form

Informed Consent template is provided under a separate cover upon request to the Sponsor.

18.4 Sample Investigator Agreement

Sample Investigator Agreement will be provided under a separate cover upon request to the Sponsor.

18.5 List of Consumables and Accessories

INFUSION SETS

MMT-386	MiniMed Quick-set 80cm tubing with 9mm cannula (box of 10)
MMT-965	MiniMed Mio 80cm tubing with 6mm cannula (box of 10)
MMT-975	MiniMed Mio 80cm tubing with 9mm cannula (box of 10)

INFUSION SET INSERTION DEVICES

MMT-305QS	MiniMed Quick-serter (for use with Quick Set Infusion Sets)

RESERVOIRS

MMT-326A	1.8 mL reservoirs (box of 10)
MMT-332A	3.0 mL reservoirs (box of 10)

OTHER

N/A	Roche Accu-Chek Strips
N/A	Roche Accu-Check Solution
ACC-LR6	AA Battery (Alkaline)
MMT-174	Tape HMS-174 ADH IV3000 1-hand 13L
MMT-7015WW	Guardian Sensor 3 Over tape
HMS-180	Skin Tac Adhesive Wipe (box of 50)
MMT-7747	USB cable and wall-powered adapter
N/A	Urinary pregnancy test, if needed

18.6 Questionnaires

The questionnaires are available, when possible, in local language and will be provided under a separate cover if a request is made to the Sponsor.

19. Version History

Version	Summary of changes	Justification of changes	Potential impact of the change on performance, effectiveness, or safety or other endpoints	Identification of the affected study documents	Author(s)/Title
A	Not Applicable, New Document	Not Applicable, New Document	Not Applicable, New Document	Not Applicable, New Document	[redacted] Medical Writer
B	• Added investigational Roche meter and updated relevant sections throughout • Updated software versions for MiniMed 780G insulin pump and MiniMed Clinical app and updated relevant sections throughout • Removed language in 13.1 Clinical Events Committee Review • Updated device deficiency language in 12.1 Definitions and Classifications of Adverse Events • Updated CIP to match most current corporate CIP template • Typo/formatting corrections throughout document	• To include additional device used during study • To update software version used during study • To clarify how CEC will perform assessments and update device deficiency definition to match ISO14155:2020 definition	None	None	[redacted] Medical Writer

Version	Summary of changes	Justification of changes	Potential impact of the change on performance, effectiveness, or safety or other endpoints	Identification of the affected study documents	Author(s)/Title
C	• See "Attachment 1: CIP339 Description of Protocol Changes Version B to C" for details on changes • Added CareLink Clinical App and updated relevant sections throughout • Removed Blue Bluetooth Low Energy Adapter and updated relevant sections throughout • Updated "Table 3. Device Accountability Requirements" to update requirements for Guardian Sensor 3 • Updated visit day for Visit 3 and visit windows for Visit 5, Visit 6 , and Visit 7 • Typo/formatting corrections throughout document	• To include additional app used during study • To remove device that will not be used during study • To clarify requirements for Guardian Sensor 3 • To update visit day and windows	None	None	[redacted] Sr. Medical Writer

Version	Summary of changes	Justification of changes	Potential impact of the change on performance, effectiveness, or safety or other endpoints	Identification of the affected study documents	Author(s)/Title
D	• See "Attachment 1: CIP339 Description of Protocol Changes Version C to D" for details on changes • Added product (Klue Health App release tag 2.0) and clarification for endpoint analysis • Increased number of subjects to enroll and complete • Increased duration of subject participation • Added subject repeat participation • Increased overall study duration • Adjusted visit days and visit windows for Visit 2 through Visit 7 • Updated meals for at-home baseline and in-clinic meal challenge • Added device re-use disclosure • Typo/formatting/wording corrections throughout document	• To add product for use in the study • To allow for more subjects and subject repeat participation in the study • To optimize visit days and visit windows • To include additional meals/beverages during the meal challenge • To clarify device re-use • To correct/clarify CIP language	• Clarifications made to endpoints	• Updates required for informed consent and investigator's brochure	[redacted] Sr. Medical Writer

Version	Summary of changes	Justification of changes	Potential impact of the change on performance, effectiveness, or safety or other endpoints	Identification of the affected study documents	Author(s)/Title
E	• See "Attachment 1: CIP339 Description of Protocol Changes Version D to E" for details on changes • Typo/formatting/wording corrections throughout document • Added product [redacted] • Revised device re-use disclosure	• [redacted] • To correct/clarify CIP language • To clarify device re-use	• None	• Updates required for informed consent	[redacted] Sr. Medical Writer

Version	Summary of changes	Justification of changes	Potential impact of the change on performance, effectiveness, or safety or other endpoints	Identification of the affected study documents	Author(s)/Title
F	• See "Attachment 1: CIP339 Description of Protocol Changes Version E to F" for details on changes • Updated "Duration" • Updated "Schedule of Events" [redacted] ○ Removed breakfast meal challenge on Day 4 (at home and in-clinic) ○ Updated window for Visit 3 ○ Updated questionnaire timing • [redacted] • Updated "Table 4. Study Visit Details" • Typo/formatting corrections throughout document	See "Attachment 1: CIP339 Description of Protocol Changes Version E to F" for details		Updates required for informed consent	[redacted] Sr. Medical Writer