Medtronic	
Study Title	Evaluation of the MiniMed™ 780G System in Type 1 Adult and Pediatric Subjects Utilizing Insulin Fiasp® (Insulin Aspart Injection)
NCT Number	NCT05224258
Document Description	Clinical Investigation Plan (Version E)
Document Date	07-NOV-2023

Medtronic **Clinical Investigation Plan**	
Clinical Investigation Plan (CIP)/Study Title	Evaluation of the MiniMed™ 780G System in Type 1 Adult and Pediatric Subjects Utilizing Insulin Fiasp® (Insulin Aspart Injection)
CIP Identifier	336
Health Canada Investigational Testing Authorization (ITA) Application Number	344299
Investigational Device Exemption (IDE) Number	G210307
Study Product Name & Study Product Model	• MiniMed™ 780G Insulin Pump with software Version 6.7 (MMT-1884 in US; MMT-1885XCC in Canada) - referred to as the study pump throughout this protocol • Guardian™ 4 Sensor (MMT-7040 in US; MMT-7040X1 or MMT-7040C4 in Canada) - referred to as the sensor throughout this protocol • Guardian 4 Transmitter (MMT-7841 in US; MMT-7841XW4 in Canada) • Medtronic Extended infusion set (MMT-430, MMT-431, MMT-432, MMT-433, MMT-440, MMT-441, MMT-442, and MMT-443 in US; MMT-430A, MMT-431AH, MMT-431AJ, MMT-432A, MMT-433AJ, MMT-440A, MMT-441AH, MMT-441AJ, MMT-442AH, MMT-442AJ, and MMT-443AJ in Canada) • Medtronic Extended Reservoir (MMT-342) • Fiasp® (insulin aspart injection) • One-Press Serter (MMT-7512 in US; MMT-7512WE in Canada) - referred to as the Serter throughout this protocol • Transmitter Charger (MMT-7715) • Tester (MMT-7736L) • Roche Accu-Chek™ Guide Link Glucose Meter (08116083022 [US], Kit number 08116113198M & Meter number 08109222001 [Canada]) -referred to as the Accu-Chek Guide Link study meter throughout this protocol • Medtronic CareLink™ Personal software (MMT-7333) • Medtronic CareLink system software (MMT-7350) • MiniMed Clinical App (MMT-6103 Android™ app; MMT-6104 IOS™ app) • MiniMed Mobile App (MMT-6101 Android™ app; MMT-6102 IOS™ app) • CareLink Clinical App (MMT-6113 Android™ app; MMT-6114 IOS™ app)

	• Blue Bluetooth® Low Energy Adapter (ACC-1003911D and ACC-1003911F)- referred to as the Blue Adapter in this protocol • Ketone meter to be used for blood ketone measurements only • Accu-Chek Guide test strips (07453736001 in US; 00064562312704 in Canada) • Sponsor-provided smartphone, upon request
Description of CIP	This global study (US, Canada, and Australia) will evaluate the safety and effectiveness of the MiniMed 780G system in type 1 adult and pediatric subjects utilizing Fiasp (insulin aspart injection) in a home setting.
Global Sponsor (Funding Source)	Medtronic MiniMed, Inc. ("Medtronic") 18000 Devonshire St Northridge, CA 91325 866.948.6633
Local Sponsor	Medtronic Australasia Pty. Ltd 2 Alma Road Macquarie Park, NSW 2113 Australia Medtronic Canada ULC ("Medtronic") 99 Hereford St. Brampton, Ontario, Canada
Document Version	E (Equivalent to Version E.1)
Version Date	07-NOV-2023
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1. Glossary

Abbreviations	
ADE	Adverse Device Effect
AID	Automated Insulin Delivery
ASADE	Anticipated Serious Adverse Device Effect
AE	Adverse Event
AHCL	Advanced Hybrid Closed Loop
AUC	Area Under Curve
BG	Blood Glucose
BMI	Body Mass Index
CEC	Clinical Events Committee
CFR	Code of Federal Regulations
CGM	Continuous Glucose Monitoring
CIP	Clinical Investigation Plan
CRF	Case Report Form
CSII	Continuous Subcutaneous Insulin Infusion
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DD	Device Deficiency
DKA	Diabetic Ketoacidosis
DMC	Data Monitoring Committee
DoH	Declaration of Helsinki
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EOS	End of Study
ER	Emergency Room
FDA	Food and Drug Administration
FDAAA	Food and Drug Administration Amendments Act
GCP	Good Clinical Practice
HbA1c	Glycosylated hemoglobin
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICH	International Conference of Harmonization
ICF	Informed Consent Form
ICMJE	International Committee of Medical Journal Editors
ID	Identification
IDE	Investigational Device Exemption
IFU	Instructions for Use
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITA	Investigational Testing Authorization
ITT	Intention to Treat

Abbreviations	
IV	Intravenous
MCRS	Medtronic Clinical& Regulatory Solutions
MDR	Medical Device Regulation
NGSP	National Glycohemoglobin Standardization Program
PC	Personal Computer
PI	Principal Investigator
PP	Per Protocol
QC	Quality Control
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Sensor Augmented Pump
SAP	Statistical Analysis Plan
SG	Sensor Glucose
SI	Sensor Integrity
SMBG	Self-Monitoring of Blood Glucose
SOP	Standard Operating Procedure
SR	Significant Risk
TDD	Total Daily Dose
TIR	Time in Range
TLS	Transport Layer Security
TSH	Thyroid-stimulating hormone
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect

2. Synopsis

Title	Evaluation of the MiniMed™ 780G System in Type 1 Adult and Pediatric Subjects Utilizing Insulin Fiasp® (Insulin Aspart Injection)
Clinical Study Type	Safety and Effectiveness Evaluation
Global Sponsor	[redacted] Medtronic MiniMed ("Medtronic") 18000 Devonshire St Northridge, CA 91325, USA 866.948.6633
Local Sponsor	Medtronic Australasia Pty. Ltd 2 Alma Road Macquarie Park, NSW 2113 Australia Medtronic Canada ULC ("Medtronic") 99 Hereford St. Brampton, Ontario, Canada L6Y 0R3 905 460 37211
Indication Under Investigation	Labeling for the use of Fiasp (insulin aspart injection) in the MiniMed 780G System
Products	• MiniMed™ 780G Insulin Pump with software Version 6.7 (MMT-1884 in US; MMT-1885XCC in Canada) - referred to as the study pump throughout this protocol • Guardian™ 4 Sensor (MMT-7040 in US; MMT-7040X1 or MMT-7040C4 in Canada) - referred to as the sensor throughout this protocol • Guardian 4 Transmitter (MMT-7841 in US; MMT-7841XW4 in Canada) • Medtronic Extended infusion set (MMT-430, MMT-431, MMT-432, MMT-433, MMT-440, MMT-441, MMT-442, and MMT-443 in US; MMT-430A, MMT-431AH, MMT-431AJ, MMT-432A, MMT-433AJ, MMT-440A, MMT-441AH, MMT-441AJ, MMT-442AH, MMT-442AJ, and MMT-443AJ in Canada) • Medtronic Extended Reservoir (MMT-342) • Fiasp® (insulin aspart injection) • One-Press Serter (MMT-7512 in US; MMT-7512WE in Canada) - referred to as the Serter throughout this protocol • Transmitter Charger (MMT-7715) • Tester (MMT-7736L) • Roche Accu-Chek™ Guide Link Glucose Meter (08116083022 [US], Kit number 08116113198M & Meter number 08109222001 [Canada]) -referred to as the Accu-Chek Guide Link study meter throughout this protocol • Medtronic CareLink™ Personal software (MMT-7333) • Medtronic CareLink system software (MMT-7350) • MiniMed Clinical App (MMT-6103 Android™ app; MMT-6104 IOS™ app)

	• MiniMed Mobile App (MMT-6101 Android™ app; MMT-6102 IOS™ app) • CareLink Clinical App (MMT-6113 Android™ app; MMT-6114 IOS™ app) • Blue Bluetooth® Low Energy Adapter (ACC-1003911D and ACC-1003911F)- referred to as the Blue Adapter in this protocol • Ketone meter to be used for blood ketone measurements only • Accu-Chek Guide test strips (07453736001 in US; 00064562312704 in Canada) • Sponsor-provided smartphone, upon request
Purpose	The purpose of this study is to evaluate the safety and effectiveness of the MiniMed 780G system in type 1 adult and pediatric subjects utilizing Fiasp (insulin aspart injection) in a home setting
Objective(s)	The objective of this study is to evaluate the safety and effectiveness of the MiniMed 780G system utilizing insulin Fiasp (insulin aspart injection) to support product and system labeling.
Study Design	This global study is a multi-center, single arm study in insulin-requiring adult and pediatric subjects with type 1 diabetes on the MiniMed 780G system using Fiasp insulin as well as Medtronic Extended infusion set and reservoir. The run-in period and study period will be approximately 120 days long. The period from Visit 1 (consent and screening) through Visit 6 should be completed in 30 days. **Companions:** Subjects will be required to have a companion who resides (or will live) in the same building (or home) during the study at night, and also to be physically present in the same building, home or location (if not at home) during the exercise and meal challenges. A companion should be present during meal challenges and for 4 hours following the start of the meal. Companions should be able to check SMBG, give glucose and/or administer glucagon. **Run-in Period (Visits 2-6):** The run-in period begins at Visit 2 and ends once Visit 7 occurs. The intent of the run-in period will be to allow subjects to become familiar with new study devices while using their own insulin, either Humalog™ (insulin lispro injection) or NovoLog®/NovoRapid® (insulin aspart solution for injection). During the run-in period, study subjects with prior Automated Insulin Delivery (AID) control algorithm experience will be using the study pump with the SmartGuard feature activated (Auto Correction must remain OFF). and Medtronic Extended infusion set and reservoir. Subjects who do not have prior AID algorithm experience will use the system in Manual Mode. Before and during run-in period meal challenges, SmartGuard must be turned OFF, as noted in Meal Challenge instructional materials. Note for subjects who have prior experience with the Auto Mode feature in Medtronic pumps (670G/770G): The term "Auto Mode" has been replaced by the term "SmartGuard" in the 780G pump.

	During the run-in period, a 120 mg/dL (6.7 mmol/L) Auto Basal target should be set. It is recommended that Active Insulin Time is set to 4 hours. Note: The Auto Basal target setting and Active Insulin Time should be set as recommended above, unless there is a documented safety reason that would not permit these settings to be used. All subjects and their parents/caregivers as well as companions will be trained 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 and how to use glucose and glucagon in case of hypoglycemia. Parents/caregivers and companions will be instructed that they should be with the subject in the same residence or building overnight. If the MiniMed Clinical app/MiniMed Mobile app and the CareLink Clinical app are being used, parents/caregivers will be instructed that subjects should be connected to CareLink via the appropriate Smartphone app for data uploading and push notifications for low or high blood sugar when they are apart, e.g., at school, other activities. Instructions on the appropriate operation of the apps will be provided. For study purposes, subjects, companions, and parents/caregivers will be trained and/or instructed to perform self-monitoring of blood glucose (SMBG) if subjects are experiencing a severe hypoglycemic event, severe hyperglycemic event or diabetic ketoacidosis (DKA). Subjects and their parents/caregivers as well as companions will also be instructed to check blood ketones using a ketone meter if the Accu-Chek Guide Link study meter reading is greater than 300 mg/dL (16.7 mmol/L). As a precaution, subjects and their parents/caregivers will be told that they should keep their own insulin pump supplies in a safe place and to have back up supplies on hand (such as insulin and syringe, or insulin pen) 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). Subjects and their parents/caregivers will be instructed to insert sensors only in the locations that are specified in the User Guide materials. Reminders will be given to subjects at each office visit. Information about sensor insertions will be collected on an electronic case report form (eCRF) in the study database, i.e., insertion location. Subjects and their parents/caregivers will be trained on all parts of the device system. This training may include access to and use of digital online learning content. A training checklist for both subjects and parents/caregivers will be implemented and completed. The completion of emergency response training, including the use of a ketone meter, will be documented for companions. Companions may be trained in person or remotely.

	After completion of training on the study devices, subjects and their parents/caregivers may attend additional visits in the days immediately following the start of system use, as needed. They may also take advantage of having access to the digital learning content. **Study Period (Visits 7-15):** All subjects will use Fiasp for the remainder of the study and will continue using the study pump, with SmartGuard feature enabled (including Auto Correction), infusion set and reservoir for approximately 90 days during the study period. Subjects should use the system with the SmartGuard feature turned on at all times with Fiasp. When prompted by the pump, subjects should take appropriate measures and follow directions on the pump to remain in or return to the SmartGuard feature. During times when subjects are not able to use the SmartGuard feature, they should use the system in Manual Mode (e.g., Suspend before low and Suspend on low). During the first 3 weeks (between Visits 7 and 11) of the study period, a 120 mg/dL (6.7 mmol/L) Auto Basal target should be set. It is recommended that Active Insulin Time is initially set to 4 hours and then titrated towards 2-3 hours or at the investigator's discretion. During the next 3 weeks (between Visits 11 and 13) of the study period, the Auto Basal target setting should be set to 100 mg/dL (5.5 mmol/L). Active Insulin Time is recommended to be set to 2-3 hours or at investigator's discretion. During the remaining weeks of the study (any time after Visit 13) of the study period, the Auto Basal target as well as Active Insulin Time should be set to what is best for the individual subject, at investigator's discretion. Note: The Auto Basal target setting and Active Insulin Time should be set as recommended above, unless there is a documented safety reason that would not permit these settings to be used. After completion of training on the SmartGuard function, subjects and their parents/caregivers may attend additional visits in the days immediately following the start of SmartGuard use, as needed. They may also take advantage of having access to the digital learning content. **Staged Enrollment:** The enrollment of subjects 7-17 years of age will not move forward until 10 subjects 18 years or older have completed 30 days of the study period and the Data Monitoring Committee (DMC) has determined that it is safe for 7-17 year olds to be enrolled into the study. **SMBG recommendations for 780G system:**

	With the 780G system and the Guardian 4 CGM, calibration is not required. However, a calibration is optional and will occur any time a blood glucose (BG) is entered. Occasionally, subjects may receive a notification if the pump needs a BG to enter or stay in the SmartGuard feature. Subjects will be instructed to perform SMBG if their symptoms do not match the sensor glucose (SG) value (i.e., they develop symptoms of hypoglycemia or hyperglycemia, but the SG value does not correlate with their symptoms).
	
	Meal and Exercise Challenges:
	All subjects will be asked to participate in meal and exercise challenges during the run-in and study period.
	• All challenges are at least 4 hours in duration, beginning from the time when the challenge meals or exercise are started.
	• There should not be more than one meal challenge on a single day.
	• Meal and exercise challenges should not be scheduled on the same day during the specified time periods.
	
	For example: A study period regular sized or large sized meal challenge should not take place on the same day as an exercise challenge.
	
	Subjects will be asked to check BG at the start of the meal/exercise, as well as 2 hours and 4 hours after the start of the meal/exercise and provide correction insulin as necessary.
	
	Throughout the study, it is important for subjects to avoid additional meal/snack or exercise up to four hours after the start of the challenge. If additional meal/snack or exercise is needed within 4 hours after the start of the challenge, the subject will acknowledge that food intake or exercise occurred. Content and timing of the meal and exercise, along with BG values, will be recorded on a log provided by the study team.
	
	Meal challenges for all subjects (Run-in and Study period):
	
	The following meal challenges are required during the run-in and study periods:
	• Two meal challenges during the run-in period with subjects using the system in Manual Mode – between Visits 5 and 7
	  ○ Regular sized meal with missed meal bolus at lunch
	  ○ Large sized meal at breakfast, lunch or dinner
	• Two meal challenges during the study period with subjects using the system in SmartGuard, Auto Basal target set at 120 mg/dL (6.7 mmol/L) – between Visits 9 and 11 of study period
	  ○ Regular sized meal with missed meal bolus at lunch
	  ○ Large sized meal at breakfast, lunch or dinner
	• Two meal challenges during the study period with subjects using the system in SmartGuard, Auto Basal target set at 100 mg/dL (5.5 mmol/L) – between Visits 12 and 13 of study period

- Regular sized meal with missed meal bolus at lunch
- Large sized meal at breakfast, lunch or dinner

- One meal challenge during the study period with subjects using the system in SmartGuard, Auto Basal target set at currently set Auto Basal target – at any time after Visit 13 of study period
  - Large sized meal at breakfast, lunch or dinner

Meal challenges should only start if the following conditions are met:

- SMBG at start of meal is < 200 mg/dL (11.1 mmol/L)
- Sensor glucose is available.

Timing	Settings/Conditions	Meal Size	Meal Type	Notes
Run-in Period between visits 5 and 7	Manual Mode only **Missed meal bolus**	Regular sized meal	Lunch	Meal content, meal size and time of meal consumption should be established so that regular sized meal challenges during the study period can be matched
Run-in Period between visits 5 and 7	Manual Mode only	Large sized meal	Breakfast Lunch or Dinner	Meal content, meal size and time of meal consumption should be established so that large sized meal challenges during the study period can be matched
Study Period, between Visits 9 and 11	SmartGuard (120 mg/dL [6.7 mmol/L] setpoint) **Missed Meal bolus**	Regular sized meal	Lunch	Meal content, meal size and time of meal consumption should match regular meal taken during run-in and the regular meal taken at the 100 mg/dL (5.5 mmol/L) setpoint
Study Period, between Visits 9 and 11	SmartGuard (120 mg/dL [6.7 mmol/L] setpoint)	Large sized meal	Breakfast, Lunch or Dinner	Meal content, meal size and time of meal consumption should match meal at Setpoint of 100 mg/dL (5.5 mmol/L) and run-in period meal
Study Period, between Visits 12 and 13	SmartGuard (100 mg/dL [5.5 mmol/L] setpoint) **Missed meal bolus**	Regular sized meal	Lunch	Meal content, meal size and time of meal consumption should match regular meal taken during run-in and the regular meal taken at the 120 mg/dL (6.7 mmol/L).

Study Period, between Visits 12 and 13	SmartGuard (100 mg/dL [5.5 mmol/L] setpoint)	Large sized meal	Breakfast Lunch or Dinner	Meal content, meal size and time of meal consumption should match meal at Setpoint of 120 mg/dL (6.7 mmol/L) and run-in period large sized meal
Study Period Any time after Visit 13	SmartGuard (with current Auto Basal target setpoint)	Large sized meal	Breakfast Lunch or Dinner	Meal content, meal size and time of meal consumption should match large meal at Setpoint of 120 mg/dL (6.7 mmol/L)/100 mg/dL (5.5 mmol/L) and run-in period large sized meals

Regular Sized Meal Challenge with Missed Meal Bolus:

Between Visits 5 and 7 for the run-in period, while subjects are in Manual Mode with CGM, they will be asked to consume a meal without administration of a Meal Bolus at lunch. The size of the meal should be equivalent to what subjects would normally eat at this mealtime.

During the study period, once at each Auto Basal setpoint (i.e. 120 mg/dL[6.7 mmol/L] and 100 mg/dL[5.5 mmol/L]), subjects will be asked to consume the same regular sized lunch meal that they had during the run-in period. For example, if the regular sized meal was consumed without an insulin bolus for the meal at 12 pm during the run-in period, that same regular sized meal should be consumed at approximately the same time of day at each setpoint during the study period.

Large sized Meal Challenges:

On large sized meal challenge days, subjects will be instructed to eat at least 1 meal with at least 50% higher caloric intake including 50% more carbohydrates and 50% higher in fat. It is recommended that subjects eat food at restaurants or consume prepared meals. The FoodPrint™ phone app (as well as questions that will be asked by the investigational center staff during visits following meal challenges) will be used to collect information about type of food, name of restaurant (if applicable), subject confirmation that the meal eaten was different from any meal eaten within the last month and subject confirmation that meal size was at least 50% more than when subjects usually consume in terms of calories, carbohydrates and fat. The timing of the meal challenges will be at the investigator's discretion. The subject's parent/caregiver should be physically present in the same building, home or location (if not at home) during the meal challenge (and for 4 hours following the start of the meal), must be able to check SMBG (in case it is needed), and give glucose/administer glucagon as needed.

Exercise Challenge for all subjects (Study Period only):

The following exercise challenges are required during the study period:

- 2 exercise challenges at setpoint of 120 mg/dL (6.7 mmol/L, between Visits 9 and 11 of the study period)
- 2 exercise challenges at setpoint of 100 mg/dL (5.5 mmol/L, between Visits 12 and 13 of the study period)
- 1 exercise challenge at currently set Auto Basal target, at any time after Visit 13 of the study period

Conditions at start of the exercise challenges:

- SG should be present at the start of each exercise challenge
- The investigator or his/her staff will determine the minimum BG for each subject at the start of each exercise challenge. It will be noted on the subject's exercise log.

Timing	Settings/Conditions	Exercise duration	Notes
Study Period, between Visits 9 and 11	SmartGuard (120 mg/dL [6.7 mmol/L] setpoint)	Min 30 minutes, up to 1.5 hours	Challenge must take place on days without meal challenge
Study Period, between Visits 9 and 11	SmartGuard (120 mg/dL [6.7 mmol/L] setpoint)	Min 30 minutes, up to 1.5 hours	Challenge must take place on days without meal challenge
Study Period, between Visits 12 and 13	SmartGuard (100 mg/dL [5.5 mmol/L] setpoint)	Min 30 minutes, up to 1.5 hours	Challenge must take place on days without meal challenge
Study Period, between Visits 12 and 13	SmartGuard (100 mg/dL [5.5 mmol/L] setpoint)	Min 30 minutes, up to 1.5 hours	Challenge must take place on days without meal challenge
Study Period Any time after Visit 13	SmartGuard (with current Auto Basal target setpoint)	Min 30 minutes, up to 1.5 hours	Challenge must take place on days without meal challenge

Exercise Challenges Details:

To fulfill the exercise challenge requirement, subjects will be asked to engage in 0.5 up to 1.5 hours of physical exercise. During this time, subjects should use either the Auto Basal setpoint target of 100 mg/dL (5.5 mmol/L) or 120 mg/dL (6.7 mmol/L) (depending on what is required at that time of the study period) unless a subject prefers to use the 150 mg/dL (8.3 mmol/L) target before, during and immediately after the exercise challenges. The FoodPrint™ phone app (as well as questions that will be asked by the investigational center staff during visits following exercise challenges) will be used to collect information about exercise type, date, time (start and finish of exercise), duration and name of the parents/caregivers/ companion

<table>
<tr><td></td><td>present. The timing of the exercise challenge will be at the investigator's discretion. A photograph should be taken on each day of the exercise challenges to indicate where the exercise took place. Subjects may also use a Smartphone app to document their exercise. The subject's parents/caregivers/companion must be physically present in the same building, home or location (if not at home) during the exercise challenge, must be able to check SMBG (in case it is needed) and give glucose/administer glucagon as needed. Examples of types of exercise include, but are not limited to:

▪ Running
▪ Cycling
▪ Swimming
▪ Hiking
▪ Walking
▪ Games (e.g. Wii interactive video games)
▪ Indoor/outdoor playground (Pediatric subjects)
▪ Yoga/stretching
▪ Any sport activity that involves ongoing physical movement (e.g., tennis, golf, basketball, volleyball, soccer)
▪ Dancing
▪ Zumba
▪ Aerobics
▪ Spinning</td></tr>
<tr><td>Sample Size and Investigational Centers</td><td>A total of up to 250 subjects with insulin-requiring type 1 diabetes age 7-80 will be enrolled at up to 25 investigational centers across the United States, Canada, and Australia in order to have 200 subjects enter the study period. Up to 125 subjects will be enrolled in the pediatric age group (7-17 years of age), up to 125 in the adult age group (18 years or older):

<table>
<tr><th>Subject Age Group</th><th>Sub-groups</th><th>Enrollment Goal (N)</th></tr>
<tr><td rowspan="3">Pediatric
Age 7 – 17 years</td><td>All Pediatric</td><td>Minimum 100 Subjects</td></tr>
<tr><td>Age 7 - 13 years</td><td>Minimum 20 Subjects</td></tr>
<tr><td>Age 14 - 17 years</td><td>Minimum 20 Subjects</td></tr>
<tr><td>Adult
Age 18 - 80 years</td><td>N/A</td><td>Minimum 100 Subjects</td></tr>
</table>

A minimum of 10 subjects and a maximum of 40 subjects is targeted for enrollment at each investigational center to ensure that the results from the individual investigational center may be pooled for analysis.

Investigational centers will be encouraged to enroll a study population that represents a wide variety of backgrounds.</td></tr>
</table>

Duration	The study is anticipated to last approximately 24 months from first investigational center initiation to study completion. Individual subject participation is expected to be approximately 120 days.
Inclusion Criteria	1. Age 7 - 80 years at time of screening. 2. Has a clinical diagnosis of type 1 diabetes: a. 14 - 80 years of age: A clinical diagnosis of type 1 diabetes for 2 years or more as determined via medical record or source documentation by an individual qualified to make a medical diagnosis. b. 7 - 13 years of age: A clinical diagnosis of type 1 diabetes for 1 year or more as determined via medical record or source documentation by an individual qualified to make a medical diagnosis. 3. Does not require a legally authorized representative to consent on their behalf due to mental or intellectual disability. 4. Subject or parent/caregiver is literate and able to read one of the languages offered in the pump. 5. Subject and/or legally authorized representative is willing to provide informed consent for participation. 6. Is willing to perform fingerstick blood glucose measurements as needed. 7. Is willing to wear the system continuously throughout the study. 8. Must have a minimum daily insulin requirement (Total Daily Dose) of greater than or equal to 8 units and maximum total daily dose of 250 units or less. 9. Has a Glycosylated hemoglobin (HbA1c) less than 10% (as processed by Central Lab) at time of screening visit. **Note:** All HbA1c blood specimens will be sent to and tested by a National Glycohemoglobin Standardization Program (NGSP) certified Central Laboratory. HbA1c testing must follow NGSP standards. 10. Has thyroid-stimulating hormone (TSH) in the normal range OR if the TSH is out of normal reference range the Free T3 is below or within the lab's reference range and Free T4 is within the normal reference range. 11. Uses pump therapy for greater than 6 months prior to screening (with or without CGM experience) 12. Is willing to upload data from the study pump, must have Internet access, and a computer system, or compatible smartphone that meets the requirements for uploading the study pump. 13. Is willing to take one of the following insulins and can financially support the use of either of the 2 insulin preparations as required during the run-in period: a. Humalog (insulin lispro injection) b. NovoLog/NovoRapid (insulin aspart injection) 14. Is willing to take Fiasp insulin during the study period (supplied via Sponsor).
Exclusion Criteria	1. Has hypersensitivity to insulin aspart or one of the excipients in Fiasp. 2. Has a history of 2 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 3. Has been hospitalized or has visited the ER in the 6 months prior to screening resulting in a primary diagnosis of uncontrolled diabetes.

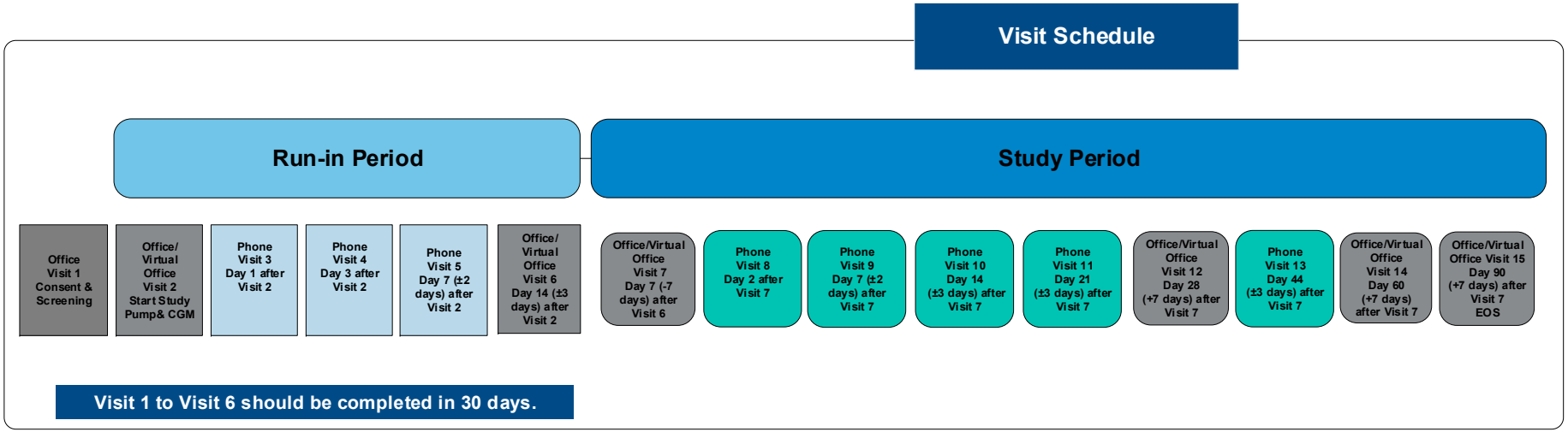
	4. Has had DKA in the last 6 months prior to screening visit. 5. Will not tolerate tape adhesive in the area of sensor placement as assessed by a qualified individual. 6. Has any unresolved adverse skin condition in the area of sensor placement (e.g., psoriasis, dermatitis herpetiformis, rash, Staphylococcus infection). 7. Is female of child-bearing potential and result of pregnancy test is positive at screening. 8. Is sexually active female of child-bearing potential and is not using a form of contraception deemed reliable by the investigator. 9. Is female and plans to become pregnant during the course of the study. 10. Is being treated for hyperthyroidism at time of screening. 11. Has diagnosis of adrenal insufficiency. 12. Has taken any oral, injectable, or intravenous (IV) glucocorticoids within 8 weeks from time of screening visit, or plans to take any oral, injectable, or IV glucocorticoids during the course of the study. 13. Is using hydroxyurea at time of screening or plans to use it during the study. 14. 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. 15. Is currently abusing illicit drugs. 16. Is currently abusing marijuana. 17. Is currently abusing prescription drugs. 18. Is currently abusing alcohol. 19. Using pramlintide (Symlin), DPP-4 inhibitor, liraglutide (Victoza or other GLP-1 agonists), metformin, canagliflozin (Invokana or other SGLT2 inhibitors) at time of screening. 20. 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. 21. Has elective surgery planned that requires general anesthesia during the course of the study. 22. Has sickle cell disease, hemoglobinopathy; or has received red blood cell transfusion or erythropoietin within 3 months prior to time of screening. 23. Plans to receive red blood cell transfusion or erythropoietin over the course of study participation. 24. Is diagnosed with current eating disorder such as anorexia or bulimia. 25. Has been diagnosed with chronic kidney disease that results in chronic anemia. 26. Has a hematocrit that is below the normal reference range of lab used. 27. Is on dialysis. 28. Has serum creatinine of >2 mg/dL. 29. Has celiac disease that is not adequately treated as determined by the investigator. 30. 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. 31. Has had history of cardiovascular event 1 year or more from the time of screening without

	a. a normal EKG and stress test within 6 months prior to screening or during screening or b. clearance from a qualified physician prior to receiving the study devices if there is an abnormal EKG or stress test. 32. Has 3 or more cardiovascular risk factors listed below without a normal EKG within 6 months prior to screening or during screening or clearance from a qualified physician if there is an abnormal EKG: • Age >35 years • Type 1 diabetes of >15 years' duration • Presence of any additional risk factor for coronary artery disease • Presence of microvascular disease (proliferative retinopathy or nephropathy, including microalbuminuria) • Presence of peripheral vascular disease • Presence of autonomic neuropathy 33. Is a member of the research staff involved with the study. 34. Has used a MiniMed 780G pump prior to screening.
Study Visit Schedule	Subjects may participate in up to 15 planned study visits, as presented below in **Synopsis Figure 1**, for approximately 120 days of device wear. Virtual office visit (audio visual) may be performed for office visits in cases where an office visit is not possible. For detailed information, see Section 9.1.1. Visit 1 to Visit 6 should be completed in 30 days. • Visit 1 (Office): Consent and screening **<u>Run-In:</u>** • Visit 2 (Office/Virtual Office): Start Run-In ○ Eligibility has been confirmed ○ Start study pump and CGM ○ Register and upload study pump in CareLink Personal and CareLink system • Visit 3 (Phone): Day 1 after Visit 2 – Required for subjects without CGM or closed loop experience; as needed for all others ○ Ask subjects and their parents/caregivers if they require assistance, e.g., additional training ○ Ask subjects about adverse events and device performance ○ Review CareLink reports • Visit 4 (Phone): Day 3 after Visit 2 – Required for subjects without CGM or closed loop experience; as needed for all others ○ Ask subjects and their parents/caregivers if they require assistance, e.g., additional training ○ Ask subjects about adverse events and device performance ○ Review CareLink reports • Visit 5 (Phone): Day 7 (±2 days) after Visit 2 ○ Ask subjects and their parents/caregivers if they require assistance, e.g., additional training ○ Ask subjects about adverse events and device performance

	○ Review CareLink reports ○ Remind subjects about run-in period meal challenge • Visit 6 (Office/Virtual Office): Day 14 (±3 days) after Visit 2 ○ Ask subjects about adverse events and device performance ○ Review CareLink reports ○ Visit 6 and 7 may be combined **Study Period:** • Visit 7 (Office/Virtual Office): Start Study Period, Day 7 (-7 days) after Visit 6 ○ Ask subjects about adverse events and device performance ○ Review CareLink reports ○ Start Auto Basal target at 120 mg/dL (6.7 mmol/L) setpoint with Active Insulin Time set to 4 hours, titrate towards 2-3 hours or at investigator's discretion ○ Turn on SmartGuard with Auto Corrections "ON" ○ Instruct subjects about the required meal and exercise challenges for both the 100 mg/dL (5.5 mmol/L) and 120 md/dL (6.7 mmol/L) setpoint between Visits 9 and 13 of the study period • Visit 8 (Phone): Day 2 after Visit 7 – Required for subjects without CGM or closed loop experience; as needed for all others ○ Adjust pump settings as needed ○ Ask subjects and their parents/caregivers if they require assistance, e.g., additional training ○ Ask subjects about adverse events and device performance ○ Review CareLink reports ○ Remind subjects about meal/exercise challenges for 120 mg/dL (6.7 mmol/L) setpoint • Visit 9 (Phone): Day 7 (±2 days) after Visit 7 ○ Adjust pump settings as needed ○ Ask subjects about adverse events and device performance ○ Review CareLink reports ○ Remind subjects about meal/exercise challenges for 120 mg/dL (6.7 mmol/L) setpoint • Visit 10 (Phone): Day 14 (±3 days) after Visit 7 ○ Adjust pump settings as needed ○ Ask subjects about adverse events and device performance ○ Review CareLink reports ○ Instruct subjects about the required meal/exercise challenges for 120 mg/dL (6.7 mmol/L) setpoint • Visit 11 (Phone): Day 21 (±3 days) after Visit 7 ○ Adjust pump settings as needed ○ Ask subjects about adverse events and device performance ○ Review CareLink reports ○ Change Auto Basal target to 100 mg/dL (5.5 mmol/L) setpoint with Active Insulin Time set to 2-3 hours or at investigator's discretion ○ Remind subjects about meal/exercise challenges for 100 mg/dL (5.5 mmol/L) setpoint

	• Visit 12 (Office/Virtual Office): Day 28 (+7 days) after Visit 7
	  ○ Ask subjects about adverse events and device performance
	  ○ Review CareLink reports
	• Visit 13 (Phone): Day 44 (±3 days) after Visit 7
	  ○ Adjust Auto Basal target with Active Insulin Time at investigator's discretion
	  ○ Ask subjects about adverse events and device performance
	  ○ Review CareLink reports
	  ○ Remind subjects about meal/exercise challenges
	• Visit 14 (Office/Virtual Office): Day 60 (+7 days) after Visit 7
	  ○ Ask subjects about adverse events and device performance
	  ○ Review CareLink reports
	• Visit 15 (Office/Virtual Office): Day 90 (+7 days) after Visit 7
	  ○ Ask subjects about adverse events and device performance
	  ○ Review CareLink reports
	  ○ Return study devices
	  ○ End of Study (EOS)

Synopsis Figure 1. Visit Schedule



Safety and Monitoring/Risk Analysis	Safety monitoring and risk analysis details are described in **Section 9.4.**
Device Deficiencies	Subject and investigational center reports of device deficiencies (DDs) will be collected on electronic Case Report Forms (eCRFs) reported by subjects and/or investigational centers for device troubleshooting and device complaints. For additional information, see **Section 13**.
Statistical Analysis for Endpoints and Hypothesis	**<u>During Study Period</u>** Safety and effectiveness endpoints will be evaluated independently for ages 18-80 and ages 7-17. **Primary Safety Endpoint** • Age 18-80: The overall mean change in HbA1c from baseline to end of 3-month study period. The goal is to show non-inferiority with a margin of 0.4% comparing to a threshold of -0.5% in reducing HbA1c from baseline to end of 3-month study period. • Age 7-17: The overall mean change in HbA1c from baseline to end of 3-month study period. The goal is to show non-inferiority with a margin of 0.4% comparing to a threshold of -0.38% in reducing HbA1c from baseline to end of 3-month study period. **Primary Effectiveness Endpoint** • Age 18-80: The mean % of time in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared to a threshold of 73.7% by a non-inferiority test with a margin of 7.5% and a significance level of 0.025 (one-sided). • Age 7-17: The mean % of time in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared to a threshold of 65.3% by a non-inferiority test with a margin of 7.5% and a significance level of 0.025 (one-sided). **Secondary Effectiveness Endpoints** • Age 18-80: The mean % of time in hypoglycemia (< 54 mg/dL [3.0 mmol/L]) will be estimated and compared to a threshold of 0.86% by a non-inferiority test with a margin of 2% and a significance level of 0.025 (one-sided). • Age 18-80: The mean % of time in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared to a threshold of 73.7% by a simple superiority test and a significance level of 0.025 (one-sided). • Age 7-17: The mean % of time in hypoglycemia (< 54 mg/dL [3.0 mmol/L]) will be estimated and compared to a threshold of 0.71% by a non-inferiority test with a margin of 2% and a significance level of 0.025 (one-sided).

- Age 7-17: The mean % of time in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared to a threshold of 65.3% by a simple superiority test and a significance level of 0.025 (one-sided).

[redacted]

Safety Data Summarized

- Serious Adverse Events (SAE)
- Serious Adverse Device Effects (SADE)
- Unanticipated Adverse Device Effects
- Unanticipated Serious Adverse Device Effect
- Incidence of Severe Hypoglycemia
- Incidence of Severe Hyperglycemia
- Incidence of DKA

	Device Deficiencies Descriptive summary will be used to characterize DDs: • All reports of device issues. [redacted]
Final Report	The study results will be summarized and presented in the final report.

3. Introduction

3.1 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 (CGM), including sensor-augmented pump therapy, experience improvements in glycemic control. Advanced sensor-augmented insulin pumps are now being used in clinical practice including closed loop systems that automatically adjust the amount of insulin delivered to maintain glucose levels near the target value set by the user.[1]

The MiniMed 780G system is a closed loop insulin system. In addition to automatically adjusting the amount of insulin delivered based on sensor glucose (SG) readings while operating in the SmartGuard feature, the MiniMed 780G insulin pump can also automatically deliver correction boluses when the system has been delivering at the maximum allowable basal rate and SG remains elevated. This pump is currently in commercial distribution in Canada, Australia, and the United States. Previous clinical investigations involved the 670G Version 4.0 pump (contains the 780G AHCL algorithm) used in combination with the Guardian Sensor (3) glucose sensor, Guardian Link 3 transmitter, Humalog and Novolog insulin. This investigation is intended to confirm safety and effectiveness of the 780G insulin pump used in combination with Fiasp insulin. Additional details for non-clinical/clinical testing are provided in the report of prior investigations/ Investigator's Brochure (IB).

3.2 Purpose

The purpose of this study is to evaluate the safety and effectiveness of the MiniMed 780G system in type 1 adult and pediatric subjects utilizing Fiasp (insulin aspart injection) in a home setting.

4. Objectives and Endpoints

4.1 Objectives

The objective of this study is to evaluate the safety and effectiveness of the MiniMed 780G system utilizing insulin Fiasp (insulin aspart injection) to support product and system labeling.

4.2 Endpoints

Safety and effectiveness endpoints will be evaluated independently for ages 18-80 and ages 7-17.

4.2.1 Primary Safety Endpoint

- Age 18-80: The overall mean change in HbA1c from baseline to end of 3-month study period. The goal is to show non-inferiority with a margin of 0.4% comparing to a threshold of -0.5% in reducing HbA1c from baseline to end of 3-month study period.
- Age 7-17: The overall mean change in HbA1c from baseline to end of 3-month study period. The goal is to show non-inferiority with a margin of 0.4% comparing to a threshold of -0.38% in reducing HbA1c from baseline to end of 3-month study period.

4.2.2 Primary Effectiveness Endpoint

- Age 18-80: The mean % of time in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared to a threshold of 73.7% by a non-inferiority test with a margin of 7.5% and a significance level of 0.025 (one-sided).
- Age 7-17: The mean % of time in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared to a threshold of 65.3% by a non-inferiority test with a margin of 7.5% and a significance level of 0.025 (one-sided).

4.2.3 Secondary Effectiveness Endpoint

- Age 18-80: The mean % of time in hypoglycemia (< 54 mg/dL [3.0 mmol/L]) will be estimated and compared to a threshold of 0.86% by a non-inferiority test with a margin of 2% and a significance level of 0.025 (one-sided).
- Age 18-80: The mean % of time in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared to a threshold of 73.7% by a simple superiority test and a significance level of 0.025 (one-sided).
- Age 7-17: The mean % of time in hypoglycemia (< 54 mg/dL [3.0 mmol/L]) will be estimated and compared to a threshold of 0.71% by a non-inferiority test with a margin of 2% and a significance level of 0.025 (one-sided).
- Age 7-17: The mean % of time in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared to a threshold of 65.3% by a simple superiority test and a significance level of 0.025 (one-sided).

4.2.5 **Safety Data Summarized**

Serious Adverse Events (SAE)

Serious Adverse Device Effects (SADE)

Unanticipated Adverse Device Effects

- Unanticipated Serious Adverse Device Effect

Incidence of Severe Hypoglycemia

Incidence of Severe Hyperglycemia

Incidence of DKA

4.2.6 Device Deficiencies

Descriptive summary will be used to characterize DDs:

- All reports of device issues.

[redacted]

[redacted]

5. Study Design

This global study is a multi-center, single arm study in insulin-requiring adult and pediatric subjects with type 1 diabetes on the MiniMed 780G system using Fiasp insulin as well as Medtronic Extended infusion set and reservoir. The run-in period and study period will be approximately 120 days long.

The period from Visit 1 (consent and screening) through Visit 6 should be completed in 30 days.

Companions:

Subjects will be required to have a companion who resides (or will live) in the same building (or home) during the study at night, and also to be physically present in the same building, home or location (if not at home) during the exercise and meal challenges. A companion should be present during meal challenges and for 4 hours following the start of the meal. Companions should be able to check SMBG, give glucose and/or administer glucagon.

Run-in Period (Visits 2-6):
The run-in period begins at Visit 2 and ends once Visit 7 occurs.

The intent of the run-in period will be to allow subjects to become familiar with new study devices while using their own insulin, either Humalog™ (insulin lispro injection) or NovoLog®/NovoRapid® (insulin aspart solution for injection). During the run-in period, study subjects with prior Automated Insulin

Delivery (AID) control algorithm experience will be using the study pump with the SmartGuard feature activated (Auto Correction must remain OFF). and Medtronic Extended infusion set and reservoir. Subjects who do not have prior AID algorithm experience will use the system in Manual Mode. Before and during run-in period meal challenges, SmartGuard must be turned OFF, as noted in Meal Challenge instructional materials.
Note for subjects who have prior experience with the Auto Mode feature in Medtronic pumps (670G/770G): The term "Auto Mode" has been replaced by the term "SmartGuard" in the 780G pump.

During the run-in period, a 120 mg/dL (6.7 mmol/L) Auto Basal target should be set. It is recommended that Active Insulin Time is set to 4 hours.

Note: The Auto Basal target setting and Active Insulin Time should be set as recommended above, unless there is a documented safety reason that would not permit these settings to be used.

All subjects and their parents/caregivers as well as companions will be trained 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 and how to use glucose and glucagon in case of hypoglycemia.

Parents/caregivers and companions will be instructed that they should be with the subject in the same residence or building overnight.

If the MiniMed Clinical app/MiniMed Mobile app and the CareLink Clinical app are being used, parents/caregivers will be instructed that subjects should be connected to CareLink via the appropriate Smartphone app for data uploading and push notifications for low or high blood sugar when they are apart, e.g., at school, other activities. Instructions on the appropriate operation of the apps will be provided.

For study purposes, subjects, companions, and parents/caregivers will be trained and/or instructed to perform self-monitoring of blood glucose (SMBG) if subjects are experiencing a severe hypoglycemic event, severe hyperglycemic event or diabetic ketoacidosis (DKA). Subjects and their parents/caregivers as well as companions will also be instructed to check blood ketones using a ketone meter if the Accu-Chek Guide Link study meter reading is greater than 300 mg/dL (16.7 mmol/L).

As a precaution, subjects and their parents/caregivers will be told that they should keep their own insulin pump supplies in a safe place and to have back up supplies on hand (such as insulin and syringe, or insulin pen) 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).

Subjects and their parents/caregivers will be instructed to insert sensors only in the locations that are specified in the User Guide materials. Reminders will be given to subjects at each office visit. Information about sensor insertions will be collected on an electronic case report form (eCRF) in the study database, i.e., insertion location.

Subjects and their parents/caregivers will be trained on all parts of the device system. This training may include access to and use of digital online learning content. A training checklist for both subjects and parents/caregivers will be implemented and completed.

The completion of emergency response training, including the use of a ketone meter, will be documented for companions. Companions may be trained in person or remotely.

After completion of training on the study devices, subjects and their parents/caregivers may attend additional visits in the days immediately following the start of system use, as needed. They may also take advantage of having access to the digital learning content.

Study Period (Visits 7-15):
All subjects will use Fiasp for the remainder of the study and will continue using the study pump, with SmartGuard feature enabled (including Auto Correction), infusion set and reservoir for approximately 90 days during the study period.

Subjects should use the system with the SmartGuard feature turned on at all times with Fiasp. When prompted by the pump, subjects should take appropriate measures and follow directions on the pump to remain in or return to the SmartGuard feature. During times when subjects are not able to use the SmartGuard feature, they should use the system in Manual Mode (e.g., Suspend before low and Suspend on low).

During the first 3 weeks (between Visits 7 and 11) of the study period, a 120 mg/dL (6.7 mmol/L) Auto Basal target should be set. It is recommended that Active Insulin Time is initially set to 4 hours and then titrated towards 2-3 hours or at the investigator's discretion.

During the next 3 weeks (between Visits 11 and 13) of the study period, the Auto Basal target setting should be set to 100 mg/dL (5.5 mmol/L). Active Insulin Time is recommended to be set to 2-3 hours or at investigator's discretion.

During the remaining weeks of the study (any time after Visit 13) of the study period, the Auto Basal target as well as Active Insulin Time should be set to what is best for the individual subject, at investigator's discretion.

Note: The Auto Basal target setting and Active Insulin Time should be set as recommended above, unless there is a documented safety reason that would not permit these settings to be used.

After completion of training on the SmartGuard function, subjects and their parents/caregivers may attend additional visits in the days immediately following the start of SmartGuard use, as needed. They may also take advantage of having access to the digital learning content.

Staged Enrollment:
The enrollment of subjects 7-17 years of age will not move forward until 10 subjects 18 years or older have completed 30 days of the study period and the Data Monitoring Committee (DMC) has determined that it is safe for 7-17 year olds to be enrolled into the study.

SMBG recommendations for 780G system:
With the 780G system and the Guardian 4 CGM, calibration is not required. However, a calibration is optional and will occur any time a blood glucose (BG) is entered. Occasionally, subjects may receive a notification if the pump needs a BG to enter or stay in the SmartGuard feature. Subjects will be instructed to perform SMBG if their symptoms do not match the sensor glucose (SG) value (i.e., they develop symptoms of hypoglycemia or hyperglycemia, but the SG value does not correlate with their symptoms).

Meal and Exercise Challenges:
All subjects will be asked to participate in meal and exercise challenges during the run-in and study period.

- All challenges are at least 4 hours in duration, beginning from the time when the challenge meals or exercise are started.
- There should not be more than one meal challenge on a single day.
- Meal and exercise challenges should not be scheduled on the same day during the specified time periods.

For example: A study period regular sized or large sized meal challenge should not take place on the same day as an exercise challenge.

Subjects will be asked to check BG at the start of the meal/exercise, as well as 2 hours and 4 hours after the start of the meal/exercise and provide correction insulin as necessary.

Throughout the study, it is important for subjects to avoid additional meal/snack or exercise up to four hours after the start of the challenge. If additional meal/snack or exercise is needed within 4 hours after the start of the challenge, the subject will acknowledge that food intake or exercise occurred. Content and timing of the meal and exercise, along with BG values, will be recorded on a log provided by the study team.

Meal challenges for all subjects (Run-in and Study period):

The following meal challenges are required during the run-in and study periods:

- Two meal challenges during the run-in period with subjects using the system in Manual Mode – between Visits 5 and 7
    - Regular sized meal with missed meal bolus at lunch

- Large sized meal at breakfast, lunch or dinner

- Two meal challenges during the study period with subjects using the system in SmartGuard, Auto Basal target set at 120 mg/dL (6.7 mmol/L) – between Visits 9 and 11 of study period
  - Regular sized meal with missed meal bolus at lunch
  - Large sized meal at breakfast, lunch or dinner
- Two meal challenges during the study period with subjects using the system in SmartGuard, Auto Basal target set at 100 mg/dL (5.5 mmol/L) – between Visits 12 and 13 of study period
  - Regular sized meal with missed meal bolus at lunch
  - Large sized meal at breakfast, lunch or dinner
- One meal challenge during the study period with subjects using the system in SmartGuard, Auto Basal target set at currently set Auto Basal target – at any time after Visit 13 of study period
  - Large sized meal at breakfast, lunch or dinner

Meal challenges should only start if the following conditions are met:

- SMBG at start of meal is < 200 mg/dL (11.1 mmol/L)
- Sensor glucose is available.

Timing	Settings/Conditions	Meal Size	Meal Type	Notes
Run-in Period between visits 5 and 7	Manual Mode only **Missed meal bolus**	Regular sized meal	Lunch	Meal content, meal size and time of meal consumption should be established so that regular sized meal challenges during the study period can be matched
Run-in Period between visits 5 and 7	Manual Mode only	Large sized meal	Breakfast Lunch or Dinner	Meal content, meal size and time of meal consumption should be established so that large sized meal challenges during the study period can be matched
Study Period, between Visits 9 and 11	SmartGuard (120 mg/dL [6.7 mmol/L] setpoint) **Missed Meal bolus**	Regular sized meal	Lunch	Meal content, meal size and time of meal consumption should match regular meal taken during run-in and the regular meal taken at the 100 mg/dL (5.5 mmol/L) setpoint
Study Period, between Visits 9	SmartGuard (120 mg/dL [6.7 mmol/L] setpoint)	Large sized meal	Breakfast, Lunch or Dinner	Meal content, meal size and time of meal consumption should match meal at Setpoint

and 11				of 100 mg/dL (5.5 mmol/L) and run-in period meal
Study Period, between Visits 12 and 13	SmartGuard (100 mg/dL [5.5 mmol/L] setpoint) **Missed meal bolus**	Regular sized meal	Lunch	Meal content, meal size and time of meal consumption should match regular meal taken during run-in and the regular meal taken at the 120 mg/dL (6.7 mmol/L).
Study Period, between Visits 12 and 13	SmartGuard (100 mg/dL [5.5 mmol/L] setpoint)	Large sized meal	Breakfast Lunch or Dinner	Meal content, meal size and time of meal consumption should match meal at Setpoint of 120 mg/dL (6.7 mmol/L) and run-in period large sized meal
Study Period Any time after Visit 13	SmartGuard (with current Auto Basal target setpoint)	Large sized meal	Breakfast Lunch or Dinner	Meal content, meal size and time of meal consumption should match large meal at Setpoint of 120 mg/dL (6.7 mmol/L)/100 mg/dL (5.5 mmol/L) and run-in period large sized meals

Regular Sized Meal Challenge with Missed Meal Bolus:

Between Visits 5 and 7 for the run-in period, while subjects are in Manual Mode with CGM, they will be asked to consume a meal without administration of a Meal Bolus at lunch. The size of the meal should be equivalent to what subjects would normally eat at this mealtime.

During the study period, once at each Auto Basal setpoint (i.e. 120 mg/dL[6.7 mmol/L] and 100 mg/dL[5.5 mmol/L]), subjects will be asked to consume the same regular sized lunch meal that they had during the run-in period. For example, if the regular sized meal was consumed without an insulin bolus for the meal at 12 pm during the run-in period, that same regular sized meal should be consumed at approximately the same time of day at each setpoint during the study period.

Large sized Meal Challenges:

On large sized meal challenge days, subjects will be instructed to eat at least 1 meal with at least 50% higher caloric intake including 50% more carbohydrates and 50% higher in fat. It is recommended that subjects eat food at restaurants or consume prepared meals. The FoodPrint™ phone app (as well as questions that will be asked by the investigational center staff during visits following meal challenges) will be used to collect information about type of food, name of restaurant (if applicable), subject confirmation that the meal eaten was different from any meal eaten within the last month and subject confirmation

that meal size was at least 50% more than when subjects usually consume in terms of calories, carbohydrates and fat. The timing of the meal challenges will be at the investigator's discretion. The subject's parent/caregiver should be physically present in the same building, home or location (if not at home) during the meal challenge (and for 4 hours following the start of the meal), must be able to check SMBG (in case it is needed), and give glucose/administer glucagon as needed.

Exercise Challenge for all subjects (Study Period only):

The following exercise challenges are required during the study period:

- 2 exercise challenges at setpoint of 120 mg/dL (6.7 mmol/L, between Visits 9 and 11 of the study period)
- 2 exercise challenges at setpoint of 100 mg/dL (5.5 mmol/L, between Visits 12 and 13 of the study period)
- 1 exercise challenge at currently set Auto Basal target, at any time after Visit 13 of the study period

Conditions at start of the exercise challenges:

- SG should be present at the start of each exercise challenge
- The investigator or his/her staff will determine the minimum BG for each subject at the start of each exercise challenge. It will be noted on the subject's exercise log.

Timing	Settings/Conditions	Exercise duration	Notes
Study Period, between Visits 9 and 11	SmartGuard (120 mg/dL [6.7 mmol/L] setpoint)	Min 30 minutes, up to 1.5 hours	Challenge must take place on days without meal challenge
Study Period, between Visits 9 and 11	SmartGuard (120 mg/dL [6.7 mmol/L] setpoint)	Min 30 minutes, up to 1.5 hours	Challenge must take place on days without meal challenge
Study Period, between Visits 12 and 13	SmartGuard (100 mg/dL [5.5 mmol/L] setpoint)	Min 30 minutes, up to 1.5 hours	Challenge must take place on days without meal challenge

Study Period, between Visits 12 and 13	SmartGuard (100 mg/dL [5.5 mmol/L] setpoint)	Min 30 minutes, up to 1.5 hours	Challenge must take place on days without meal challenge
Study Period Any time after Visit 13	SmartGuard (with current Auto Basal target setpoint)	Min 30 minutes, up to 1.5 hours	Challenge must take place on days without meal challenge

Exercise Challenges Details:

To fulfill the exercise challenge requirement, subjects will be asked to engage in 0.5 up to 1.5 hours of physical exercise. During this time, subjects should use either the Auto Basal setpoint target of 100 mg/dL (5.5 mmol/L) or 120 mg/dL (6.7 mmol/L) (depending on what is required at that time of the study period) unless a subject prefers to use the 150 mg/dL (8.3 mmol/L) target before, during and immediately after the exercise challenges. The FoodPrint™ phone app (as well as questions that will be asked by the investigational center staff during visits following exercise challenges) will be used to collect information about exercise type, date, time (start and finish of exercise), duration and name of the parents/caregivers/ companion present. The timing of the exercise challenge will be at the investigator's discretion. A photograph should be taken on each day of the exercise challenges to indicate where the exercise took place. Subjects may also use a Smartphone app to document their exercise. The subject's parents/caregivers/companion must be physically present in the same building, home or location (if not at home) during the exercise challenge, must be able to check SMBG (in case it is needed) and give glucose/administer glucagon as needed. Examples of types of exercise include, but are not limited to:

- Running
- Cycling
- Swimming
- Hiking
- Walking
- Games (e.g. Wii interactive video games)
- Indoor/outdoor playground (Pediatric subjects)
- Yoga/stretching
- Any sport activity that involves ongoing physical movement (e.g., tennis, golf, basketball, volleyball, soccer)
- Dancing

- Zumba
- Aerobics
- Spinning

5.1 Duration

The study is anticipated to last approximately 24 months from first investigational center initiation to study completion. Individual subject participation is expected to be approximately 120 days.

5.2 Rationale

Previous clinical investigations have confirmed the safety and clinical performance of the 780G insulin pump when used to delivery Humalog or Novolog/NovoRapid U100 insulin to patients 7- 80 years of age. In-silico modeling provided in 10977370DOC (Faster Insulin Aspart [Fiasp] Compared to Insulin Aspart - In-Silico Studies with MiniMed 670G HCL) indicates that the use of Fiasp U100 insulin with the MiniMed 670G pump will result in similar outcomes to those associated with use Humalog or Novolog/NovoRapid U100 insulin. These results provide a preliminary confirmation of the safety of using Fiasp with the 780G insulin pump. This investigation is intended to provide additional confirmation of the safety of the 780G insulin pump used in combination with Fiasp U100 insulin in humans.

6. Product Description

6.1 Intended Use

The MiniMed 780G system is intended for use by people seven years and older with type 1 diabetes who require at least 8 units of insulin per day.

6.2 General Overview of MiniMed 780G Insulin Pump System Components and Consumables

Table 1. MiniMed 780G Insulin Pump: System Components and consumable materials

Device name*	MDT Model number/ part number	US Device Regulatory Status	Canada Device Regulatory Status
MiniMed 780G Insulin Pump, Software Version 6.7 – *referred to as study pump throughout this protocol*	MMT-1884 (US) MMT-1885XCC (Canada)	Investigational	Investigational
Guardian 4 Sensor- *referred to as the sensor throughout this protocol*	MMT-7040 (US) MMT-7040X1 or MMT-7040C4 (Canada)	Non-Investigational*****	Investigational
Guardian 4 Transmitter	MMT-7841 (US) MMT-7841XW4 (Canada)	Non-Investigational*****	Investigational
Medtronic Extended infusion set	MMT-430, MMT-431, MMT-432, MMT-433, MMT-440, MMT-441, MMT-442, and MMT-443 (US) MMT-430A, MMT-431AH, MMT-431AJ, MMT-432A, MMT-433AJ, MMT-440A, MMT-441AH, MMT-441AJ, MMT-442AH, MMT-442AJ, and MMT-443AJ (Canada)	Non-Investigational	Non-Investigational*****
Medtronic Extended Reservoir	MMT-342	Non-Investigational	Licensed

Device name*	MDT Model number/ part number	US Device Regulatory Status	Canada Device Regulatory Status
One-Press Serter	MMT-7512 (US) MMT-7512WE (Canada)	Non-Investigational	Class I Medical Device****
Charger	MMT-7715	Non-Investigational	Licensed
Tester	MMT-7736L	Non-Investigational	Licensed
Medtronic CareLink Personal software	MMT-7333	Non-Investigational**	Non-Investigational; Not regulated as a medical device in Canada
Medtronic CareLink system software	MMT-7350	Non-Investigational**	Non-Investigational; Not regulated as a medical device in Canada
Roche Accu-Chek Guide Link Glucose Meter- *referred to as the Accu-Chek Guide Link study meter throughout this protocol*	08116083022 (US) Kit number 08116113198M (Canada) Meter model number 08109222001 (Canada)	Non-Investigational	Non-Investigational
MiniMed Clinical App	MMT-6103 Android; MMT-6104 IOS	Non-Investigational***	Non-Investigational; Not regulated as a medical device in Canada
MiniMed Mobile App	MMT-6101 Android; MMT-6102 IOS	Non-Investigational***	Non-Investigational; Not regulated as a medical device in Canada
CareLink Clinical App	MMT-6113 Android; MMT-6114 IOS	Non-Investigational***	Non-Investigational; Not regulated as a medical device in Canada
Blue Adapter	ACC-1003911D and ACC-1003911F	Non-Investigational	N/A
Ketone meter	N/A	Non-Investigational	Approved

Drug name*	MDT Model number/ part number	US Drug Regulatory Status	Canada Drug Regulatory Status
Fiasp (insulin aspart injection)	N/A	Approved	Approved

* For detailed information on the characteristics' materials, see device instructions for use (IFU).
** Class I Exempt
*** Class II Exempt
**** Does not have an associated license number
***** The commercial labeled stock will be disbursed after depletion of investigational labeled stock products.

Table 2. Estimated Numbers of Devices Per Subject During The Entire Study

Item	Units per Subject
MiniMed 780G Insulin Pump	1
Guardian 4 Sensor (Boxes of 5)	6
Guardian 4 Transmitter Kit (includes serter, charger, and tester)	1
Medtronic Extended infusion set (Each or Boxes of 10)	30 each or 3 boxes
Medtronic Extended Reservoir (Boxes of 10)	6
Roche Accu-Chek Guide Link Study Meter	1-2
Ketone Meter	1-2

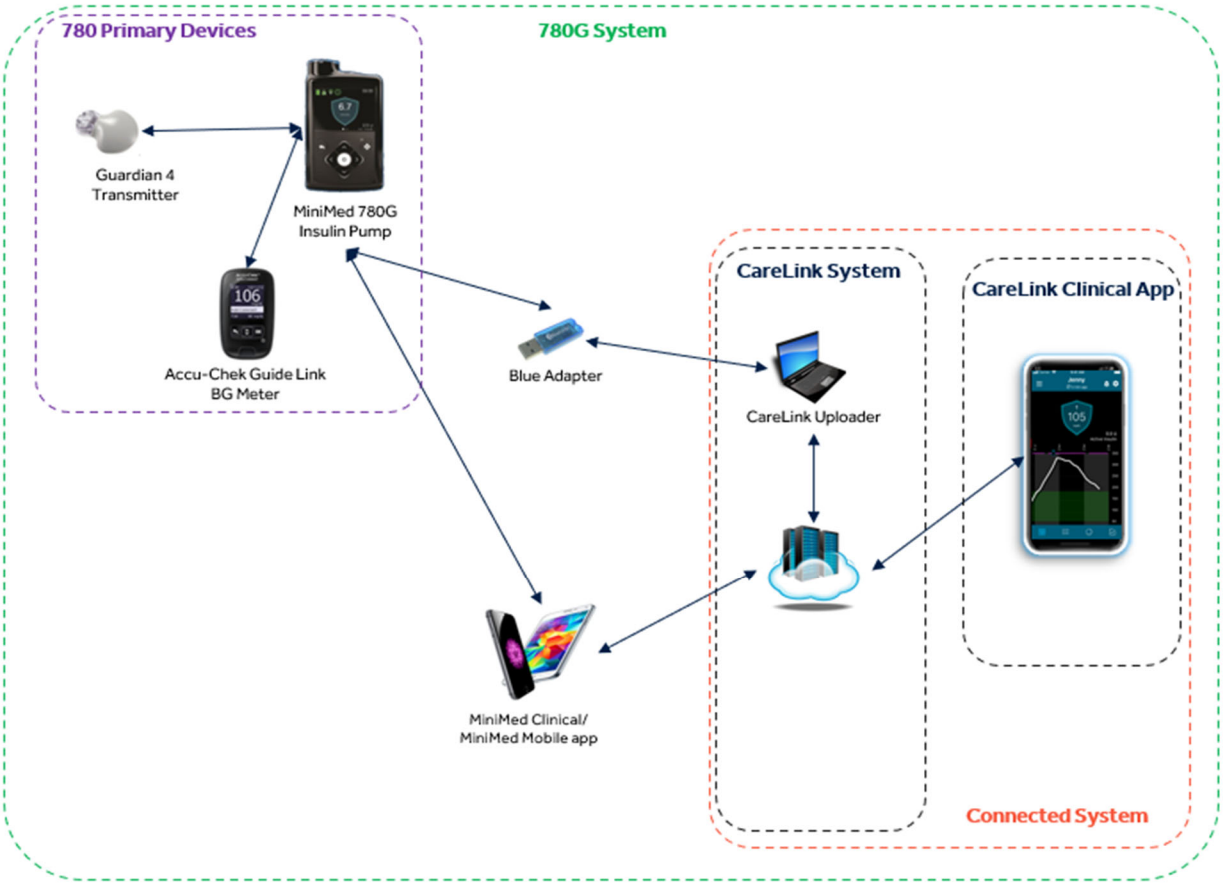
6.3 MiniMed 780G Insulin Pump

The MiniMed 780G Insulin Pump, with software Version 6.7, 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.

In this study, the MiniMed 780G Pump will be used outside of its approved intended use and in combination with the following devices:

- The MiniMed 780G Pump receives the SG values and sensor integrity (SI) check from the Guardian 4 Transmitter, which is connected to the Guardian 4 Sensor.
- The MiniMed 780G Pump receives BG values from the Roche's Accu-Chek Guide Link BG meter
- The MiniMed 780G Pump transmits data to a compatible consumer electronic device with the MiniMed Clinical app/MiniMed Mobile 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 Personal/CareLink system software through the Blue Adapter/ MiniMed Clinical app/MiniMed Mobile app.

Figure 1. 780G System and Components



6.4 Guardian 4 Sensor

The Guardian 4 sensor, referred to as the sensor in this protocol, is a sensor that contains one microelectrode with a thin coating of glucose oxidase beneath several layers of biocompatible membrane. The Guardian 4 sensor will be used with the 780G system. The sensor is the latest generation of glucose sensor with design changes for 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.

6.5 Guardian 4 Transmitter

The Guardian 4 Transmitter is a portable, electrical current meter intended to process, store, and transmit glucose sensor values to the compatible insulin pump. The transmitter sends SG values and SI data from the sensor to compatible insulin pumps via a Bluetooth Low Energy wireless communication protocol.

6.6 Medtronic Extended Infusion Set

Infusion sets are single-use by patients with diabetes mellitus requiring subcutaneous administered insulin to maintain acceptable BG levels. The Medtronic Extended infusion set is an infusion set with a pre-loaded inserter, inserted into the subcutaneous tissue of a user, and is connected to a Medtronic MiniMed medication reservoir (for use with a Medtronic MiniMed insulin pump). There are three basic components of the infusion set:

1. Catheter hub with cannula and adhesive patch
2. Tubing
3. Tubing connector

The cannula, connected to the catheter hub, is introduced into subcutaneous tissue (i.e., infusion site). The tubing connects the catheter hub and the tubing connector to provide the fluid from the medication reservoir housed within the insulin pump.

The device utilizes a new high-performance tubing connector (H-Cap) to replace the current proprietary Paradigm connector (P-Cap), an extended wear tubing to replace the current tubing, and an extended wear adhesive patch. **Figure 2** and **Figure 3** illustrate the device and the tubing connectors.

The Medtronic Extended infusion set enhances patient wear time to 7 days. This is done by maintaining insulin formulation stability (including physical, chemical, and microbiological stability) during infusion through the pump/infusion set system over extended time (up to 7 days).

Figure 2. Medtronic Extended infusion set

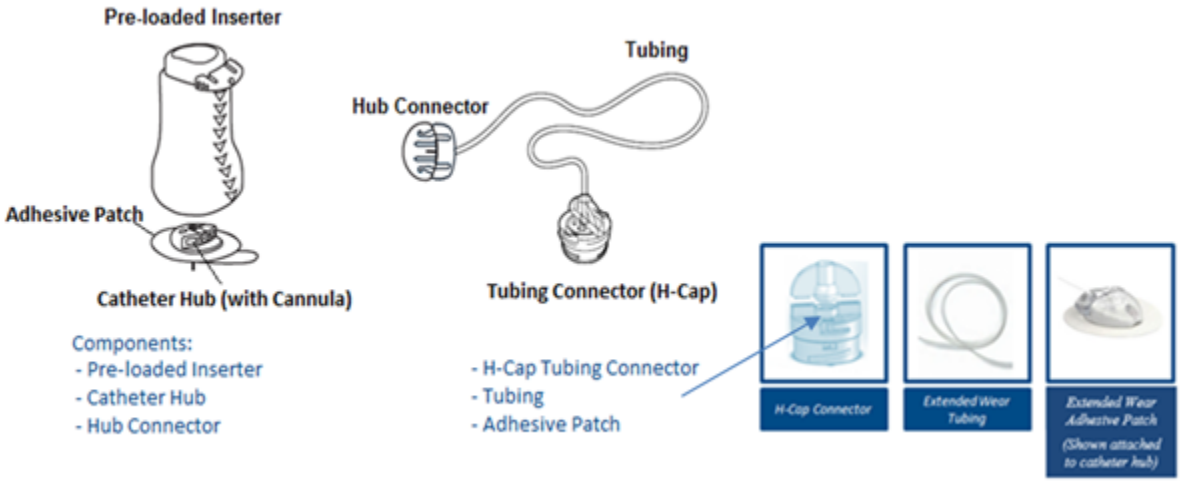
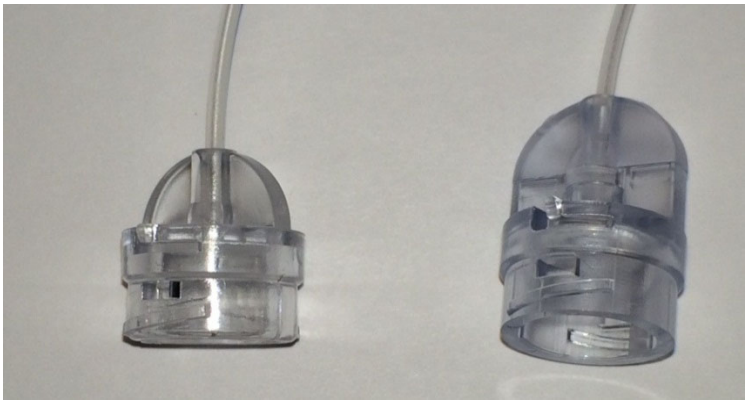


Figure 3. Connector, P-Cap (Left); High-Performance Connector, H-Cap (Right)



6.7 Medtronic Extended Reservoir

The Medtronic Extended Reservoir is indicated for the subcutaneous infusion of insulin from compatible Medtronic insulin pumps and Medtronic Extended infusion sets.

6.8 Insulin

Fiasp (insulin aspart injection) is a fast-acting insulin with the same active ingredient as Novolog/NovoRapid, used to treat adults and pediatrics with diabetes for the control of high blood sugar.

Subjects will use their own rapid-acting analogue insulin (Novolog/NovoRapid or Humalog) during the run-in period. During the study period, subjects will be provided with Fiasp for use.

6.9 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 sensor 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.

6.10 Charger

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

6.11 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.

6.12 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.

6.13 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.

6.14 Roche Accu-Chek Guide Glucose Meter

The Roche's Accu-Chek Guide Link meter is a home BG meter designed to measure and transmit 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. 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 BG meter is compatible with Roche's Accu-Chek Guide test strips.

6.15 Accessory Applications – 780G system

The MiniMed Clinical/MiniMed Mobile app is an optional accessory, which receives pump data via Bluetooth Low Energy wireless communication from the pump. The MiniMed Clinical app/MiniMed Mobile 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/MiniMed Mobile 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.

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/MiniMed Mobile screen, for remote monitoring by a care partner (e.g., caregiver). The CareLink Clinical app is not designed to monitor the performance of the insulin pump nor for direct monitoring of pump data. As a mirroring display, the app can provide notifications to the care partner via the user interface.

6.16 Blue Adapter

The Blue Adapter is an optional accessory with Bluetooth technology that facilitates the communication between a PC and the insulin pump, via a Bluetooth Low Energy wireless communication protocol. The Blue Adapter is an off-the-shelf non-medical device intended to transfer data to CareLink server. The Blue Adapter does not have any computation, diagnostic, monitoring or therapeutic function/benefit. Medtronic will provide the Blue Adapter as a convenience to subjects as an alternative for subjects when automatic uploads via the MiniMed Clinical app/MiniMed Mobile app are not possible.

6.17 Ketone Meter

The ketone meter can measure both BG (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 meter allows quantification of blood ß-Ketone levels and is the preferred patient method of testing over urine testing.

6.18 Smartphone

Sponsor may provide a smartphone, upon request.

6.19 Consumable Devices

Glucose meter accessories (e.g., Accu-Chek Guide test strips) and other consumable materials will be provided to subjects for use in the study.

6.20 Anticipated Product Changes

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

6.21 Product Accountability

Good clinical research practice requires that investigators and research teams ensure accurate accountability for any investigational devices 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 device 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/IRB) have been received.

The principal investigator (PI) 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 (US)** and **Table 4 (Canada)**.

Table 3. Device Accountability Requirements- US

Device/Drug	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	Investigational Center Return Device to Sponsor at Conclusion of Study
MiniMed 780G Insulin Pump with software Version 6.7 (MMT-1884)	Yes	Yes	Yes	Yes	Yes
Guardian 4 Sensor (MMT-7040)	Yes	Yes	Yes (Unused) No** (Used)	Yes	Yes (Unused) No** (Used)
Guardian 4 Transmitter* (MMT-7841)	Yes	Yes	Yes	Yes	Yes
Medtronic Extended infusion set (MMT-430, MMT-431, MMT-432, MMT-433, MMT-440, MMT-441, MMT-442, and MMT-443)	No	No	Yes (Complaint) No** (Non-complaint used and unused)	No	Yes (Complaint) No** (Non-complaint used and unused)
Medtronic Extended Reservoir (MMT-342)	Yes	Yes	Yes (Complaint and unused) No** (Non-complaint used)	Yes	Yes (Complaint) No** (Non-complaint used and unused)

Device/Drug	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	Investigational Center Return Device to Sponsor at Conclusion of Study
Roche Accu-Chek Guide Link Study Meter (08116083022*)	Yes	Yes	Yes	Yes	No**
Ketone meter	No	No	Yes	No	No**
Fiasp insulin	Yes	Yes	Yes (unopened vials only)	Yes	No***
Smartphone, as approved for distribution	Yes	Yes	Yes	Yes	Yes

* Devices may be combined and distributed in kits.
** If subject is unable to dispose, return products to investigational center for disposal.
If investigational center is unable to dispose, return products to sponsor for disposal.
*** Insulin leftovers should be destroyed at investigational center.

Table 4. Device Accountability Requirements- Canada

Device/Drug	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	Investigational Center Return Device to Sponsor at Conclusion of Study
MiniMed 780G Insulin Pump with software Version 6.7 (MMT-1885XCC)	Yes	Yes	Yes	Yes	Yes
Guardian 4 Sensor (MMT-7040X1 or MMT-7040C4)	Yes	Yes	Yes (Unused) No** (Used)	Yes	Yes (Unused) No** (Used)
Guardian 4 Transmitter* (MMT-7841XW4)	Yes	Yes	Yes	Yes	Yes
Medtronic Extended infusion set (MMT-430A, MMT-431AH, MMT-431AJ, MMT-432A, MMT-433AJ, MMT-440A, MMT-441AH, MMT-441AJ, MMT-442AH, MMT-442AJ, and MMT-443AJ)	Yes	Yes	Yes (Complaint and unused) No** (Non-complaint used)	Yes	Yes (Complaint and unused) No** (Non-complaint used)
Medtronic Extended Reservoir (MMT-342)	No	No	Yes (Complaint) No** (Non-complaint used and unused)	No	Yes (Complaint) No** (Non-complaint used and unused)

Device/Drug	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	Investigational Center Return Device to Sponsor at Conclusion of Study
Roche Accu-Chek Guide Link Study Meter (Kit number 08116113198M* and Meter number 08109222001)	Yes	Yes	Yes	Yes	No**
Ketone Meter	No	No	Yes	No	No**
Fiasp insulin	Yes	Yes	Yes (unopened vials only)	Yes	No***
Smartphone, as approved for distribution	Yes	Yes	Yes	Yes	Yes

*Devices may be combined and distributed in kits.
** If subject is unable to dispose, return products to investigational center for disposal.
If investigational center is unable to dispose, return products to sponsor for disposal.
*** Insulin leftovers should be destroyed at investigational center

The investigational center will promptly notify the sponsor of any device handling violation that might impact either the safety and/ or welfare of subjects or data integrity.

6.21.1 Receipt and Inventory of Study Devices by Investigational Center

- Upon receipt of the study devices, investigational center staff will take 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
- Sign and date the packing slips/invoices, noting any discrepancies, and file in appropriate study binder
- Notify the study monitor of any discrepancies
- Enter or acknowledge the study device information on the appropriate eCRF in the study database, if applicable as described in **Table 3 (US)** and **Table 4 (Canada)**.

6.21.2 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/user guide/labeling.

6.21.3 Dispensing of Study Devices

Each time a study device and insulin is dispensed to a subject by the investigator or authorized member of the research team, eCRF, and/or source documentation will be completed as required. Documentation may include:

- Dispensing date
- Subject identification (ID)
- Lot number (where applicable)
- Serial number (where applicable)

- Device type
- Amount dispensed

6.21.4 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 (US)** and **Table 4 (Canada)**. and store them in a secure environment. If containers/units/devices are missing, the reasons should be documented in the applicable eCRF and/or source document. If discrepancies between the amounts used by subjects and the amounts expected to be returned exist, the reasons should be documented in the applicable eCRF and/or source document.

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 (US)** and **Table 4 (Canada)**. The devices that are being returned to the investigational center may be returned to the sponsor as subjects complete the study, at the study closure or upon sponsor request.

Other consumable devices (e.g., alcohol wipes, study meter supplies, and tape), and accessories shipped in kits, supplies or materials may be returned to the sponsor, they may be retained by investigational centers for educational purposes only, or they may be disposed of appropriately by the 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 and/or source document must be accounted for as described above before they are returned to the sponsor.

Fiasp insulin will be accounted for at the investigational center. Any insulin that is left over will be destroyed by participating centers and destruction records will be filed.

7. Study Site Requirements

7.1 Investigator/Investigational Center Selection

In order to conduct the study, it is required that the investigator and investigational center staff have the appropriate medical training.

The primary investigator must be a physician who has managed patients on both CGM and insulin pump therapy for at least one- year and must be familiar with insulin carbohydrate ratios, insulin sensitivity, and treating diabetic emergencies.

7.2 Study Site Activation

During the activation process (prior to subject enrollment), Medtronic will train investigational center staff who may then train other staff at each investigational center. 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 requirements shall be fulfilled, including but not limited to the following:

- EC/IRB approval (and voting list, as required by local law) of the current version of the CIP Informed Consent Form (ICF), and report of prior investigations/IB
- Regulatory authority approval or notification (as required per local law)
- Fully executed Clinical Trial Agreement (CTA)
- Financial disclosure (if applicable)
- Curriculum vitae (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 PI prior to performing delegated study activities.

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

8. Selection of Subjects

8.1 Study Population

A total of up to 250 subjects with insulin-requiring type 1 diabetes age 7-80 will be enrolled at up to 25 investigational centers across the United States, Canada, and Australia in order to have 200 subjects enter the study period. Up to 125 subjects will be enrolled in the pediatric age group (7-17 years of age), up to 125 in the adult age group (18 years or older):

Subject Age Group	Sub-groups	Enrollment Goal (N)
Pediatric Age 7 – 17 years	All Pediatric	Minimum 100 Subjects
	Age 7 - 13 years	Minimum 20 Subjects
	Age 14 - 17 years	Minimum 20 Subjects
Adult Age 18 - 80 years	N/A	Minimum 100 Subjects

A minimum of 10 subjects and a maximum of 40 subjects is targeted for enrollment at each investigational center to ensure that the results from the individual investigational center may be pooled for analysis.

Investigational centers will be encouraged to enroll a study population that represents a wide variety of backgrounds.

8.2 Subject Enrollment

Subjects will be considered enrolled in the study upon signing the ICF and assent form (if applicable).

A subject will be assigned a unique study subject ID via the eCRF, which is a 9-digit code (336XXXXXX). The first three digits refer to the CIP number (336), the next three characters refer to the investigational center identifier, and the last 3 digits refer to the subject number assigned during Visit 1 (e.g., 336002001 is subject 001 from investigational center 002).

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

8.3 Inclusion Criteria

1. Age 7 - 80 years at time of screening.
2. Has a clinical diagnosis of type 1 diabetes:
    a. 14 - 80 years of age: A clinical diagnosis of type 1 diabetes for 2 years or more as determined via medical record or source documentation by an individual qualified to make a medical diagnosis.
    b. 7 - 13 years of age: A clinical diagnosis of type 1 diabetes for 1 year or more as determined via medical record or source documentation by an individual qualified to make a medical diagnosis.

3. Does not require a legally authorized representative to consent on their behalf due to mental or intellectual disability.
4. Subject or parent/caregiver is literate and able to read one of the languages offered in the pump.
5. Subject and/or legally authorized representative is willing to provide informed consent for participation.
6. Is willing to perform fingerstick blood glucose measurements as needed.
7. Is willing to wear the system continuously throughout the study.
8. Must have a minimum daily insulin requirement (Total Daily Dose) of greater than or equal to 8 units and maximum total daily dose of 250 units or less.
9. Has a Glycosylated hemoglobin (HbA1c) less than 10% (as processed by Central Lab) at time of screening visit.

   Note: All HbA1c blood specimens will be sent to and tested by a National Glycohemoglobin Standardization Program (NGSP) certified Central Laboratory. HbA1c testing must follow NGSP standards.

10. Has thyroid-stimulating hormone (TSH) in the normal range OR if the TSH is out of normal reference range the Free T3 is below or within the lab's reference range and Free T4 is within the normal reference range.
11. Uses pump therapy for greater than 6 months prior to screening (with or without CGM experience)
12. Is willing to upload data from the study pump, must have Internet access, and a computer system, or compatible smartphone that meets the requirements for uploading the study pump.
13. Is willing to take one of the following insulins and can financially support the use of either of the 2 insulin preparations as required during the run-in period:
    a. Humalog (insulin lispro injection)
    b. NovoLog/NovoRapid (insulin aspart injection)
14. Is willing to take Fiasp insulin during the study period (supplied via Sponsor).

8.4 Exclusion Criteria

1. Has hypersensitivity to insulin aspart or one of the excipients in Fiasp.
2. Has a history of 2 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

3. Has been hospitalized or has visited the ER in the 6 months prior to screening resulting in a primary diagnosis of uncontrolled diabetes.
4. Has had DKA in the last 6 months prior to screening visit.
5. Will not tolerate tape adhesive in the area of sensor placement as assessed by a qualified individual.
6. Has any unresolved adverse skin condition in the area of sensor placement (e.g., psoriasis, dermatitis herpetiformis, rash, Staphylococcus infection).
7. Is female of child-bearing potential and result of pregnancy test is positive at screening.
8. Is sexually active female of child-bearing potential and is not using a form of contraception deemed reliable by the investigator.
9. Is female and plans to become pregnant during the course of the study.
10. Is being treated for hyperthyroidism at time of screening.
11. Has diagnosis of adrenal insufficiency.
12. Has taken any oral, injectable, or intravenous (IV) glucocorticoids within 8 weeks from time of screening visit, or plans to take any oral, injectable, or IV glucocorticoids during the course of the study.
13. Is using hydroxyurea at time of screening or plans to use it during the study.
14. 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.
15. Is currently abusing illicit drugs.
16. Is currently abusing marijuana.
17. Is currently abusing prescription drugs.
18. Is currently abusing alcohol.
19. Using pramlintide (Symlin), DPP-4 inhibitor, liraglutide (Victoza or other GLP-1 agonists), metformin, canagliflozin (Invokana or other SGLT2 inhibitors) at time of screening.

20. 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.
21. Has elective surgery planned that requires general anesthesia during the course of the study.
22. Has sickle cell disease, hemoglobinopathy; or has received red blood cell transfusion or erythropoietin within 3 months prior to time of screening.
23. Plans to receive red blood cell transfusion or erythropoietin over the course of study participation.
24. Is diagnosed with current eating disorder such as anorexia or bulimia.
25. Has been diagnosed with chronic kidney disease that results in chronic anemia.
26. Has a hematocrit that is below the normal reference range of lab used.
27. Is on dialysis.
28. Has serum creatinine of >2 mg/dL.
29. Has celiac disease that is not adequately treated as determined by the investigator.
30. 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.
31. Has had history of cardiovascular event 1 year or more from the time of screening without
    a. a normal EKG and stress test within 6 months prior to screening or during screening or
    b. clearance from a qualified physician prior to receiving the study devices if there is an abnormal EKG or stress test.
32. Has 3 or more cardiovascular risk factors listed below without a normal EKG within 6 months prior to screening or during screening or clearance from a qualified physician if there is an abnormal EKG:
    - Age >35 years
    - Type 1 diabetes of >15 years' duration
    - Presence of any additional risk factor for coronary artery disease
    - Presence of microvascular disease (proliferative retinopathy or nephropathy, including microalbuminuria)
    - Presence of peripheral vascular disease
    - Presence of autonomic neuropathy
33. Is a member of the research staff involved with the study.
34. Has used a MiniMed 780G pump prior to screening.

9. Study Procedures

9.1 Schedule of Events

Subjects may participate in up to 15 planned study visits, as presented in **Figure 4 (Section 9.1.1)** for approximately 120 days of device wear. Virtual office visit (audio visual) may be performed for office visits in cases where an office visit is not possible. The exit visit should occur at the office, unless an emergent situation occurs.

If the subject visits the investigational center outside of the scheduled study visits, a Visit eCRF will be completed to document the reason for the unscheduled visit.

Refer to **Section 9.1.1**, **Table 5** for the Visit Details.

If subject exits the study early (i.e., before their last scheduled visit), HbA1c requirements that apply to the final visit will be completed for subjects who have completed Visit 7. Refer to CIP336 Questionnaire Guide for collection of early exit requirements.

The Exit eCRF and all associated activities should be completed for all subjects who have withdrawn, discontinued, or completed the study.

9.1.1 Study Visit Schedule & Scheduled Follow-Up Visit Windows

Visit 1 to Visit 6 should be completed in 30 days.

- Visit 1 (Office): Consent and screening

Run-In:

- Visit 2 (Office/Virtual Office): Start Run-In
    - Eligibility has been confirmed
    - Start study pump and CGM
    - Register and upload study pump in CareLink Personal and CareLink system
- Visit 3 (Phone): Day 1 after Visit 2 – Required for subjects without CGM or closed loop experience; as needed for all others

- Ask subjects and their parents/caregivers if they require assistance, e.g., additional training
- Ask subjects about adverse events and device performance
- Review CareLink reports

- Visit 4 (Phone): Day 3 after Visit 2 – Required for subjects without CGM or closed loop experience; as needed for all others
  - Ask subjects and their parents/caregivers if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
- Visit 5 (Phone): Day 7 (±2 days) after Visit 2
  - Ask subjects and their parents/caregivers if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Remind subjects about run-in period meal challenge
- Visit 6 (Office/Virtual Office): Day 14 (±3 days) after Visit 2
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Visit 6 and 7 may be combined

Study Period:

- Visit 7 (Office/Virtual Office): Start Study Period,
  Day 7 (-7 days) after Visit 6
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Start Auto Basal target at 120 mg/dL (6.7 mmol/L) setpoint with Active Insulin Time set to 4 hours, titrate towards 2-3 hours or at investigator's discretion
  - Turn on SmartGuard with Auto Corrections "ON"
  - Instruct subjects about the required meal and exercise challenges for both the 100 mg/dL (5.5 mmol/L) and 120 md/dL (6.7 mmol/L) setpoint between Visits 9 and 13 of the study period

- Visit 8 (Phone): Day 2 after Visit 7 – Required for subjects without CGM or closed loop experience; as needed for all others
    - Adjust pump settings as needed
    - Ask subjects and their parents/caregivers if they require assistance, e.g., additional training
    - Ask subjects about adverse events and device performance
    - Review CareLink reports
    - Remind subjects about meal/exercise challenges for 120 mg/dL (6.7 mmol/L) setpoint
- Visit 9 (Phone): Day 7 (±2 days) after Visit 7
    - Adjust pump settings as needed
    - Ask subjects about adverse events and device performance
    - Review CareLink reports
    - Remind subjects about meal/exercise challenges for 120 mg/dL (6.7 mmol/L) setpoint
- Visit 10 (Phone): Day 14 (±3 days) after Visit 7
    - Adjust pump settings as needed
    - Ask subjects about adverse events and device performance
    - Review CareLink reports
    - Instruct subjects about the required meal/exercise challenges for 120 mg/dL (6.7 mmol/L) setpoint
- Visit 11 (Phone): Day 21 (±3 days) after Visit 7
    - Adjust pump settings as needed
    - Ask subjects about adverse events and device performance
    - Review CareLink reports
    - Change Auto Basal target to 100 mg/dL (5.5 mmol/L) setpoint with Active Insulin Time set to 2-3 hours or at investigator's discretion
    - Remind subjects about meal/exercise challenges for 100 mg/dL (5.5 mmol/L) setpoint
- Visit 12 (Office/Virtual Office): Day 28 (+7 days) after Visit 7
    - Ask subjects about adverse events and device performance
    - Review CareLink reports
- Visit 13 (Phone): Day 44 (±3 days) after Visit 7
    - Adjust Auto Basal target with Active Insulin Time at investigator's discretion
    - Ask subjects about adverse events and device performance
    - Review CareLink reports
    - Remind subjects about meal/exercise challenges

- Visit 14 (Office/Virtual Office): Day 60 (+7 days) after Visit 7
    - Ask subjects about adverse events and device performance
    - Review CareLink reports
- Visit 15 (Office/Virtual Office): Day 90 (+7 days) after Visit 7
    - Ask subjects about adverse events and device performance
    - Review CareLink reports
    - Return study devices
    - End of Study (EOS)

Figure 4. Visit Schedule

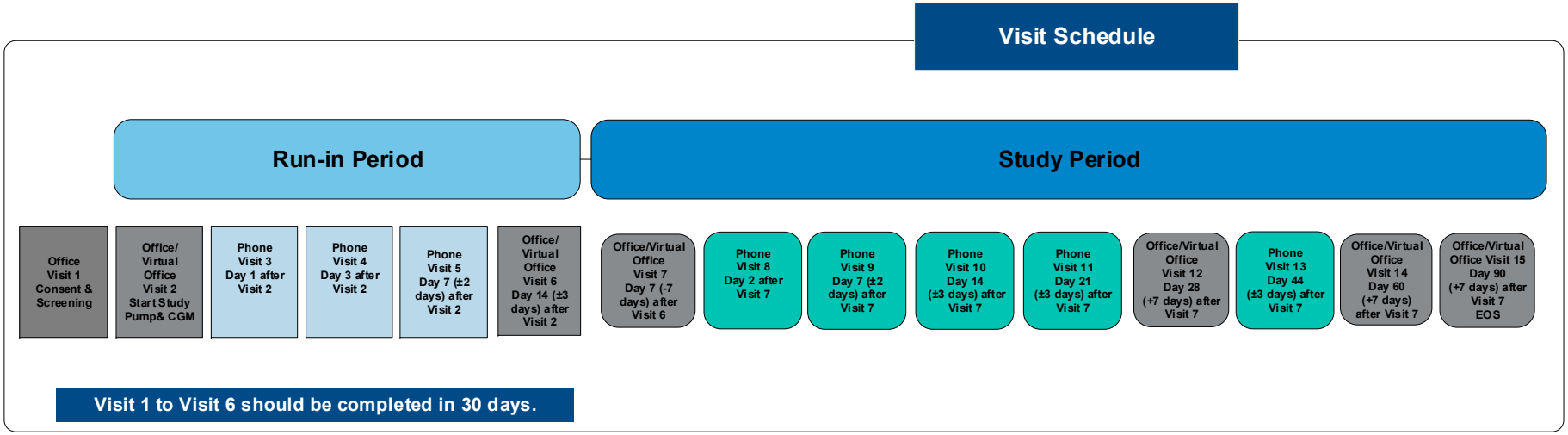


Table 5. Visit Details

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
Visit Activities and Data Collection												
Collect consent forms, e.g., ICF, Assent form (if applicable), California Experimental Subject's Bill of Rights (if applicable), HIPAA form 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											X
Collect demographic and other baseline characteristics 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 blood sample for HbA1c testing. All collected blood specimens will be sent to and tested by a NGSP certified Central	X											X

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
Laboratory. HbA1c testing must follow NGSP standards.												
Collect specimens for required lab testing: Hematocrit, Creatinine, TSH (see lab instructions for additional information)	X											
Collect information about medical history	X											
Collect information about concomitant medications	X											
Collect any changes to diabetes medications during the study		X (if applicable)	X (if applicable)	X (if applicable)	X (if applicable)	X (if applicable)	X (if applicable)	X (if applicable)	X (if applicable)	X (if applicable)	X (if applicable)	X (if applicable)
Confirm subject eligibility results, including labs, prior to moving forward with any study procedures		X										
Assist with Questionnaires - Refer to CIP336 Questionnaire Guide for administration details.		X										X
Provide study subjects with the Accu-Chek Guide Link study meter and ketone meter, including needed supplies		X			As needed	As needed	As needed	As needed	As needed	As needed	As needed	
Complete Quality Control (QC) testing of the Accu-Chek Guide Link study meter and ketone meter per respective user guide		X			As needed	As needed	As needed	As needed	As needed	As needed	As needed	

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
Train subjects and their parents/caregivers on the use of the Accu-Chek Guide Link study meter and ketone meter, refer to user guides		X										
Train companions on emergency response and the use of the ketone meter (refer to user guides)		X										
Train subjects and their parents/caregivers on the use of the 780G pump		X										
Start study subjects on the 780G insulin pump system • Subjects with prior AID experience will be using the study pump with SmartGuard feature activated (Auto Correction OFF). • Subjects who do not have prior AID algorithm experience will use the system in Manual Mode.		X										
Provide study subjects the Medtronic Extended infusion sets, reservoirs, sensors and transmitter		X			As needed	As needed	As needed	As needed	As needed	As needed	As needed	

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
Train subjects and their parents/caregivers on the Medtronic Extended infusion sets, reservoirs, sensor and transmitter		X										
Start study subjects on CGM, including transmitter, sensor and accessories		X										
Instruct subjects and their parents/caregivers to place the sensor in a location that is approved for placement per the User guide and study directions, as applicable		X	X	X	X	X	X	X	X	X	X	
Train study subjects and their parents/caregivers on the 780G SmartGuard features		X				X						
Start/continue study subjects on 780G SmartGuard with Auto Correction (as applicable). **During the study period, all SmartGuard features should be used by all subjects.**						X						
Instruct subjects and their parents/caregivers to switch from pump		X				X						

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
therapy to manual injections until issue is resolved if: • Hospital admission is needed for any reason • Glucose is persistently elevated (i.e., above 300 mg/dL [16.7 mmol/L]) and not responding to correction boluses and/or infusion set change(s) • There is an occlusion alarm with elevated glucose, where the study subject is not able to address the occlusion by changing the infusion set												
Adjust pump settings							As needed	As needed				
Create an investigational center account in the CareLink system software (see separate instructions)		X										
Create an account for study subjects in CareLink Personal (see separate instructions)		X										
Link the study subjects account to the investigational center account		X										

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
Train subjects and their parents/caregivers on the use of CareLink Personal– provide relevant set of written instructions		X										
Set up 780G system apps, if applicable: • MiniMed Clinical/MiniMed Mobile app • CareLink Clinical app		X (if applicable)										
If applicable: • Train subjects and their parents/caregivers on the use of the 780G system apps: MiniMed Clinical app/MiniMed Mobile app and CareLink Clinical app		X (if applicable)										
Instruct/Remind subjects and their parents/caregivers about the requirement to perform meal challenges during the run-in period SmartGuard should not be activated				X	X (If needed)							
Instruct/Remind subjects and their parents/caregivers about the requirement to perform meal and exercise challenges during the study period • At 120 mg/dL (6.7 mmol/L) Auto Basal Setpoint between **Visits 7 and 11** of the study period						X	X	X	X	X	X	

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
• At 100 mg/dL (5.5 mmol/L) Auto Basal Setpoint between **Visits 11 and 13** of the study period • At current Auto Basal Setpoint at any time after **Visit 13** of the study period												
Start Auto Basal target at 120 mg/dL (6.7 mmol/L setpoint with Active Insulin Time set to 4 hours, titrate towards 2-3 hours or at investigator's discretion. Turn on SmartGuard with Auto Corrections "ON". Note: The Auto Basal target setting and Active Insulin Time should be set as recommended above, unless there is a documented safety reason that would not permit these settings to be used.						X						
Change Auto Basal target to 100 mg/dL (5.5 mmol/L) setpoint with Active Insulin Time set to 2-3 hours or at investigator's discretion.								X (Visit 11)				

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
Note: The Auto Basal target setting and Active Insulin Time should be set as recommended above, unless there is a documented safety reason that would not permit these settings to be used.												
Adjust the Auto Basal target as well as Active Insulin Time should be set to what is best for the individual subject, at investigator's discretion. Note: The Auto Basal target setting and Active Insulin Time should be set as recommended above, unless there is a documented safety reason that would not permit these settings to be used.										X		
Dispense Fiasp						X			As needed		As needed	
Dispense study materials (e.g., smartphone [upon request and approval], reference guides, subject training materials, etc.)		X										

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
Dispense other study supplies as needed (e.g., alcohol swabs, adhesive remover, etc.)		X			As needed	As needed			As needed		As needed	
At all visits and/or between visits (if the investigational center is contacted), adjust insulin settings and insulin dose as needed		X	As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed	
Confirm the study pump upload data is available in CareLink system software (at office visit or day prior if phone or virtual office visit)		X		X	X	X	X	X	X	X	X	X
Print and review CareLink system reports			X	X	X	X	X	X	X	X	X	X
Review surveillance report in Medtronic's secure upload application and review with subjects as necessary			As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed	As needed
Enter data into eCRFs as required	X	X	X	X	X	X	X	X	X	X	X	X
Schedule next visit day and time	X	X	X	X	X	X	X	X	X	X	X	
Collect and destroy Fiasp												X
Collect study devices at study end (see device disposition **Table 3 [US]** and **Table 4 [Canada]** for details)												X

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
Note: If the visit must be conducted via Virtual Office, the blood tests may be collected via mobile phlebotomy service.												
Questions To Ask at Study Visits												
Ask if subjects and their parents/caregivers have general study-related questions and concerns	X	X	X	X	X	X	X	X	X	X	X	X
Ask subjects 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 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).		X	X	X	X	X	X	X	X	X	X	X

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
Ask subjects about device performance issues and if they called the investigational center staff to report them. Instruct/Remind subjects to contact the investigational center staff in the event they experience problems with their study devices.		X	X	X	X	X	X	X	X	X	X	X
Ask subjects and their parents/caregivers if they require assistance, e.g., additional training			X	X			X					
Study Subject General Training and Instructions												
Remind subjects and their parents/caregivers that the use and wear of study devices throughout the study is a requirement		X	X	X	X	X	X	X	X	X	X	
Instruct subjects on carbohydrate (CHO) counting as needed (Investigator discretion)		X	X	X	X	X	X	X	X	X	X	
Instruct subjects, their parents/caregivers, and companions on diabetes self-management principles, including the use of glucose and glucagon in the event of hypoglycemia		X										
Instruct subjects, their parents/caregivers, and companions (companions: during initial training only) that blood ketone		X	X	X	X	X	X	X	X	X	X	

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
testing is required every time BG is greater than 300 mg/dL (16.7 mmol/L), as measured by the Accu-Chek Guide Link study meter.												
Instruct subjects and their parents/caregivers to consider avoiding the use of products containing acetaminophen If medications containing acetaminophen are taken: • Wait until use of the medication is stopped before using SG to make treatment decisions • Use additional BG meter readings to verify glucose levels • While the SmartGuard feature is active, instruct subjects to use the temp target feature (when used, Auto Correction is not available) • Instruct subjects that in case of prolonged use of acetaminophen, the temp		X	X	X	X	X	X	X	X	X	X	

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
target feature can be used repeatedly and in succession												
Remind subject and their parents/caregivers to bring in both Accu-Chek Guide Link study meter and ketone meter at each required office visit.		X	X	X	X		X	X	X	X	X	
Remind subject and their parents/caregivers to keep their devices charged, as applicable		X	X	X	X	X	X	X	X	X	X	
Instruct subjects and parents/caregivers regarding the use of the Accu-Chek Guide Link study meter to make treatment decisions: • When a BG required alert is received: ○ Clear the alert and enter a BG meter reading before using the SG to make treatment decisions • When symptoms are present: ○ If SG readings are not aligned with		X	X	X	X	X	X	X	X	X	X	

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
symptoms (e.g., if a study subject is feeling low while the SG reading is not low), use the meter to confirm BG. ○ If SG readings continue to be different from symptoms, call the study doctor												
Instruct subjects and parents/caregivers to refer primary healthcare providers to the investigational center staff if they have any questions about study devices and their functions		X	X	X	X	X	X	X	X	X	X	X
Instruct subjects and their parents/caregivers that they should not assume that SmartGuard is able to prevent all hypoglycemia or all hyperglycemia including diabetic ketoacidosis		X				X						
Instruct study subjects and parents/caregivers that regular weekly uploads of the study pump is required.		X	X	X	X	X	X	X	X	X	X	

	Visit 1 (Office)	Run-In Period				Study Period						
		Visit 2 (Office or Virtual Office)	Visit 3* and 4* (Phone)	Visit 5 (Phone)	Visit 6 (Office or Virtual Office)	Visit 7 (Office or Virtual Office)	Visit 8* (Phone)	Visit 9, 10 & 11 (Phone)	Visit 12 (Office or Virtual Office)	Visit 13 (Phone)	Visit 14 (Office or Virtual Office)	Visit 15** (Office or Virtual Office)
Visit Window	**Enrollment**		**Day 1 and Day 3 after Visit 2**	**Day 7 (±2 days) after Visit 2**	**Day 14 (±3 days) after Visit 2**	**Day 7 (-7 days) after Visit 6**	**Day 2 after Visit 7**	**Day 7 (±2 days) after Visit 7 Day 14 and Day 21 (±3 days) after Visit 7**	**Day 28 (+7 days) after Visit 7**	**Day 44 (±3 days) after Visit 7**	**Day 60 (+7 days) after Visit 7**	**Day 90 (+7 days) after Visit 7 EOS**
With Bluetooth connection and the MiniMed Clinical app/MiniMed Mobile app , scheduled uploads are not required for subjects with compatible smartphones, as they are designed to occur continuously. Subjects that do not have compatible smartphones will be required to use the Blue Adapter to facilitate uploads to their computers.												
Instruct subjects and their parents/caregivers to give meal bolus of insulin 15-20 minutes prior to meals during the run-in period		X										
Instruct subjects and their parents/caregivers to give meal bolus of insulin at the start of meals during the study period						X						

** Required for subjects without CGM or closed loop experience; as needed for all others.*
***When subjects exit the study early, all requirements that are listed for the final visit apply.*

9.2 Data Collection

All data collection and study procedure requirements are described at the subject visits in **Section 9.1**.

9.3 Subject Consent

Informed Consent and assent (if applicable) will be obtained in accordance with ISO14155:2020, the Code of Federal Regulations (CFR) Title 21, Part 50 (US only) or Tri-Council Policy Statement, Article 3.2 (Canada only). Prior to entry into the study, the California Experimental Subject's Bill of Rights (if applicable, US only), the EC (Ethics Committee)/Institutional Review Board (IRB) and Medtronic approved ICF form and assent form (if an assent form is required per local regulations) and an Authorization Form required by the Health Insurance Portability and Accountability Act (HIPAA; US only) will be presented to each subject to review and sign as applicable. The subject and their parent, guardian, or legally authorized representative (as applicable) will be given ample time and offered the opportunity to review these documents away from the investigational center.

If the subject is below 18 years of age, he/she should be informed about the study to the extent compatible with the subject's understanding. Per EC/IRB, if the subject could give consent to decisions about participation in research, the investigator must obtain that consent in addition to the consent of their legally authorized representative or guardian. Consent by a legal guardian or authorized representative is only allowed for subjects who are younger than legal age according to their state/country requirements.

The following will be provided to or explained to the subject and their parent, guardian, or legally authorized representative by the investigator or designee: the purpose and duration of the study, the requirements expected to be adhered to by the subject during the study and the potential risks /potential benefits associated with participation in the study. Every attempt will be made to answer the subject's and their parent's, guardian's, or legally authorized representative's questions during the informed consent and assent process. The language used shall be as non-technical as possible and must be understandable to the subject or their parent, guardian, or legally authorized representative.

Neither the investigator, nor the investigational center staff shall coerce or unduly influence a subject or their parent, guardian, or legally authorized representative to participate or to continue to participate in the clinical study. The informed consent/assent process shall not waive or appear to waive the subject's rights. The assent, if required, should be administered according to the investigational center's Standard Operating Procedures (SOPs) and the EC/IRB instructions, as applicable.

Subjects will complete California Experimental Subject's Bill of Rights (if applicable, US only), the HIPAA Form (US only), and the ICF/assent form. The consenting process must be documented in the subject's source documents. The subject and their parent, guardian, or legally authorized representative will receive copies of the fully executed documents. A subject's participation in study procedures cannot begin before the consent process has been properly executed. When the subject decides to participate in the

study, the ICF must be signed and personally dated by the subject and investigator or authorized designee, as required by the ICF. A patient contact card will be provided to the subject.

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 and their parent, guardian, or legally authorized representative in a timely manner.

Medtronic will revise the written ICF/assent form whenever new information becomes available that may be relevant to the subject's confirmed participation in the clinical study. The revised information will be sent to the investigator for approval by the EC/IRB. After approval by the EC/IRB, a copy of this information must be provided to the participating subjects, and the informed consent/assent process as described above needs to be repeated.

If the ICF/assent form is amended during the course of the study, the EC/IRB will determine:

- Whether or not active subjects and their parent, guardian, or legally authorized representative should be re-consented at their next visit and
- Whether or not subjects who have completed the study at the time of the amendment should be re-consented .

Subjects and their parent, guardian, or legally authorized representative will be informed that qualified personnel from the investigational center, the sponsor (Medtronic), regulatory authorities such as the FDA/Health Canada and/or the EC/IRB, may have access to the clinic records that reveal their identity and health care information.

The investigational center must report the following informed consent/assent violations to their EC (if applicable)/IRB and sponsor:

- Failure to obtain informed consent/assent from subject and their parent, guardian, or legally authorized representative.
- Failure to obtain informed consent/assent prior to performing one or more study procedures.
- Failure to maintain ICFs/assent forms on file for all subjects who have provided informed consent.
- Use of an ICF/assent form that has not received approval from the EC/IRB.
- Use of an incorrect version of the ICF/assent form.

9.4 Safety Monitoring/Risk Analysis

9.4.1 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.

9.4.2 Hypoglycemic/Hyperglycemic Risk

Intervention and treatment for hypoglycemia and hyperglycemia is addressed in **Section 10.1**.

9.4.3 Calibration of CGM Risk

When an erroneous glucose value is used to calibrate a CGM, this can result in inaccurate SG values. Subjects will be trained on appropriate calibration.

9.4.4 Reuse Risk

All study devices will be single patient use.

9.4.5 Sterilization Risk

The following devices will be supplied sterilized:

- Infusion sets
- Insulin reservoirs
- Sensors

9.4.6 Misuse Risk

Comprehensive training will take place at the initiation visit for investigational center staff regarding the operation of the 780G system, to include all of its functional components and all other study devices to be used during the study at the investigational center.

9.4.7 Risk of Blood Sample Collection, Contamination from Sampling Techniques

Detailed mitigations to blood sampling risk are provided in **Section 10.1**.

9.4.8 HbA1c Risk

A Central laboratory will be used for HbA1c testing.

9.5 Glucose and Glycemia Measurements

During the course of the study, the subjects' BG levels, SG levels, HbA1c, and blood ketones will be collected using the methods outlined in this section.

9.5.1 Daily Blood Glucose

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

9.5.2 Blood Ketone Values

Blood ketones will be measured by all subjects using a ketone meter when certain conditions are met:

- When a subject is symptomatic for high blood glucose
- When sensor glucose displays a glucose value >300mg/dL (16.7 mmol/L), BG should be checked by fingerstick and, if BG is >300mg/dL (16.7 mmol/L), blood ketones should be checked.

The control solution test will be performed following the manufacturer's user guide. The investigational center staff will be trained on the use of the ketone meter per the manufacturer's instructions. All ketone measurements will be reported by study subjects.

9.5.3 Sensor Glucose Values

SG data will be collected by subject's study pump and calibrated by each subject's Accu-Chek Guide Link study meter.

9.5.4 HbA1c

HbA1c is collected at baseline and the end of subjects' participation; if subjects have completed Visit 7 and exit early, a HbA1c will be collected.

9.6 Recording Data

Data entered by the investigational center staff will be captured on eCRFs using the Electronic Data Capture (EDC) system. Original eCRFs will not be considered as source data and supporting documentation will be required. In addition, the subject will complete the questionnaires online via direct entry. In case the online link is unavailable, subjects will complete the questionnaire using a paper format (this will be source data) and subsequently the investigator or designated investigational center staff will enter the responses online. If paper format is used, the investigator or designated investigational center staff should maintain the original paper source in the subject's source file.

Electronic device data will be collected from the study pump using CareLink Personal/CareLink system software. The system uses TLS technology, which encrypts all data it stores (21 CFR Part 11 compliant). Certain data points stored in the downloaded information may also be captured on the appropriate eCRF. Electronic device data could also be collected by the MiniMed Clinical app/MiniMed Mobile app and the CareLink Clinical app.

The investigator will ensure that all eCRFs are completed promptly, completely, and accurately. Medtronic will provide detailed instructions to assist with eCRF completion. In the event of data discrepancies, investigational centers will be asked to resolve queries electronically in the EDC system; otherwise, irresolvable data-related issues will be routed to the sponsor for review and final disposition. An audit trail is maintained in the EDC system to capture any corrections or changes of the eCRFs. System backups for data stored in the EDC system will be consistent with Medtronic 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.

9.7 Deviation Handling

A deviation is any instance(s) of failure to follow, intentionally or unintentionally, the requirements of the CIP. 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. Failure to do so could result in one or all of the following:

- Investigational center disqualification
- Notification to the regulatory authorities/EC/IRB depending on the severity of the deviation and reporting requirements

The investigator should not implement any deviation from, or changes to, the CIP without agreement by the sponsor and prior review and documented approval/favorable opinion from the regulatory authority (if applicable) or EC (if applicable)/IRB, except where necessary to eliminate an immediate hazard(s) to trial subjects. The use of waivers from the CIP are prohibited in this study.

9.7.1 Documenting Requirements for Study Deviations

9.7.1.1 Unplanned CIP Deviations

The investigator may encounter the need to deviate from the CIP when necessary to protect the safety, rights or well-being of a subject in an emergency or in unforeseen situations beyond the investigator's control (e.g., subject failure to attend scheduled follow-up visits, inadvertent loss of data due to computer malfunction, inability to perform required procedures due to subject illness).

Deviations from the CIP, regardless of the reason should be documented as soon as possible, after the deviation occurs or is identified. This documentation should include deviation date, description of the deviation, the reason for deviation, and the corrective action. Refer to **Table 9 (US)** and **Table 10 (Canada)** for reporting timelines for emergency deviations.

CIP deviations should be reported as follows:

a) To the EC(if applicable)/IRB for notification/acknowledgement;
b) To the sponsor and, if required;
c) To the applicable regulatory authority (reported by sponsor).

9.7.2 Reporting Requirements for Study Deviations

All study deviations must be reported 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.

The following examples are deviations that could impact subject safety, affect the integrity of study data and/or affect subject's willingness to participate in the study. These deviations are significant and require immediate sponsor notification upon investigator awareness:

- Failure to obtain informed consent/assent, i.e., there is no documentation of consenting
- Informed consent/assent obtained after initiation of study procedures
- Continuation of a subject who did not meet all inclusion/exclusion criteria
- Performing study procedure not approved by the EC/IRB
- Failure to inform EC/IRB and sponsor of reportable AEs (see **Section 11)**
- Investigational study device dispensed without obtaining informed consent/assent

In the event the deviation involves a failure to obtain a subject's consent, or is made to protect the life or physical well-being of a subject in an emergency, the deviation must be reported to Medtronic as well as the EC/IRB ,if applicable per local regulations, within five (5) working days.

Reporting of all other study deviations should comply with:

- EC/IRB policies and/or
- local laws and/or
- regulatory authority requirements

They must be reported to Medtronic as soon as possible upon the center becoming aware of the deviation. Refer to Investigator Reports, **Table 9 (US)** and **Table 10 (Canada)** for specific deviation reporting requirements and timeframes for reporting to Medtronic, EC/IRB, and regulatory authority (if applicable).

9.7.3 **Analyzing Deviations**

Medtronic is responsible for reviewing deviations, assessing their significance, and identifying any additional corrective and/or preventive actions (e.g., amend the CIP, conduct additional training, terminate the investigation). 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.

9.8 Subject Exit, Withdrawal or Discontinuation

Subjects may choose to withdraw from the study at any time by notifying investigational center staff of their intent.

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. All study devices and supplies must be returned (as applicable) and documented both in source documents and on an eCRF. Following study exit, subjects will receive standard medical care from their own providers.

A subject will be withdrawn from the study if:

- In the opinion of the investigator, the subject's health or safety would be compromised by continuing in the study (e.g., infection at skin site, severe skin reaction to adhesive).
- In the opinion of the investigator, it is in the subject's best interest to discontinue participation in the study.
- During the course of the study, subject begins using hydroxyurea.

- During the course of the study, subject begins participation in another investigational study (drug or device).
- At the discretion of the investigator: During the study it becomes known that subjects are using a non-linked BG meter for SMBG or a system that replaces SMBG.
- During the course of the study, subject begins abusing illicit drugs.
- During the course of the study, subject begins abusing marijuana.
- During the course of the study, subject begins abusing prescription drugs.
- During the course of the study, subject begins abusing alcohol.
- During the course of the study, subject begins using pramlintide (Symlin), DPP-4 inhibitors, liraglutide (Victoza or other GLP-1 agonists), metformin, canagliflozin (Invokana or other SGLT2 inhibitors).
- During the course of the study, subject receives red blood cell transfusion or erythropoietin.
- During the course of the study, the subject demonstrates that he/she is not able to comprehend instructions for study procedures, as evaluated by the appropriate research staff.
- During the study, a subject repeatedly activates SmartGuard feature when instructed otherwise, e.g., SmartGuard feature is turned on (as applicable at the discretion of the investigator).
- During the course of the study, subject is taking oral, injectable, or IV glucocorticoids
- During the study, (female) subject becomes pregnant.
- During the study, the subject experiences one severe hypoglycemic episode, if it is related to the use of 780G system SmartGuard feature.
- During the study, the subject experiences one episode of DKA, if it is related to the use of 780G system SmartGuard feature.
- During the study, subject has a cardiovascular event or any vascular event such as stroke.

Documentation of the reason(s) leading to subject withdrawal will be kept in the subject's source documentation.

9.8.1 End of Subject Participation in Study/ Completion of Study

After the study has been completed (at Visit 15 or in case of early termination), subjects will be exited from the study. Subjects will continue to work with their physician after study exit per normal standard of care. The clinical investigation is considered completed once the last subject has exited the study.

9.8.2 Lost to Follow-Up

If a subject does not return to the site for required follow-up visit(s) and cannot be reached, the investigation site personnel should make 3 documented attempts to contact the subject by phone to verify if the subject should be considered "lost-to follow up". In the event the subject is not able to perform follow-up visits at the investigation site, subject will be considered "lost to follow up" and this

needs to be documented in the Study Exit eCRF. All efforts will be made by investigation site personnel to collect all study devices and supplies back from subject, if applicable.

9.9 Study Stopping Rules

There are no predefined study stopping rules. The study will be stopped if the Data Monitoring Committee (DMC) determines that there are significant safety issues. (See DMC **Section 12.2.**)

10. Risks and Benefits

10.1 Potential Risks

The potential residual risks and mitigations associated with the devices used during this study are listed in **Table 6**. Risks associated with the commercially available devices used in the study are listed in the associated device labeling/user guides/instructions for use or report of prior investigations/ IBs.

The clinical investigation has been designed to involve as little pain, discomfort, fear and any other foreseeable risk as possible for the subjects, and both the risk threshold and the degree of distress are specifically defined in the CIP and constantly monitored.

Table 6. Risks, Prevention and Mitigation

Risk with Fiasp	Prevention and Mitigation
For a description of risks in Fiasp, refer to the links to the insulin label in the next column (US and Canada)	**USA:** https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=208751 **Canada:** https://health-products.canada.ca/dpd-bdpp/info.do?lang=en&code=94775
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. DDs or use errors can result in	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.

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	• Instruct to check their meter glucose if their high or low symptoms do not match their sensor alerts or SG readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the SG value is not accurate. • Instruct to have glucose and glucagon 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. • Parent(s)/guardian(s)/companion(s) should be present at night with subjects. • Parent(s)/guardian(s) will be trained on study device and diabetes management principles and instructed to call investigator with problems. • Companions will be trained on diabetes management principles and emergency response training. • Parent/caregivers and companions should also be present during meal and exercise challenges.

• 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 SmartGuard feature where SG 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) should be present at night with subjects. • Parent(s)/guardian(s) will be trained on study device and diabetes management principles and instructed to call investigator with problems. • Companions will be trained on diabetes management principles and emergency response training. • Parent/caregivers and companions should also be present during meal and exercise challenges. • 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 SG readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the SG value is not accurate. • Alternative method of managing glucose levels will be available (insulin and syringe for example).

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) should be present at night with subjects. • Parent(s)/guardian(s) will be trained on study device and diabetes management principles and instructed to call investigator with problems. • Companions will be trained on diabetes management principles and emergency response training. • Parent/caregivers and companions should also be present during meal and exercise challenges. • 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 SG readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the SG value is not accurate). • Instruct to have glucose and glucagon on hand for hypoglycemia.
Risk with Sensors	**Prevention and Mitigation**
Risks with sensors may include: • Skin irritation or reaction to adhesives • Bruising • Discomfort • Redness • Bleeding • 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 sensor needle removal	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 SG readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the SG value is not accurate. • Instruct if there are no sensor values, no treatment decisions will be made until a BG is confirmed.

• Residual redness associated with adhesive and/ or tapes • Scarring • Scab • Blister • Itchiness • Inflammation • Anxiety • Incorrect SG reading results in incorrect diabetes management • Subject over-treating secondary to alarms which can result in hyperglycemia or hypoglycemia	
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:	Prevention and mitigation include: • Follow the provided user guides for insertions and care of device.

• Improper insertion may lead to device performance issue	• 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: • Potential risks associated with frequent meter testing of BG and blood ketones include discomfort and ecchymosis at tips of fingers • Potential risks associated with fingerstick testing include discomfort and bruising	Prevention and mitigation include: • Follow the provided user guides for use of the study meter with fingerstick testing. • Train on the proper use of the study meter and fingerstick testing.
Risk with Closed Loop Therapy	**Prevention and Mitigation**
Risks with Closed Loop may include:	Prevention and mitigation include: • 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 or low symptoms do not match their sensor alerts or SG readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the SG 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 and glucagon 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 to verify their glucose levels. • If acetaminophen is taken, while the SmartGuard feature is active, subjects will be instructed to use the temp target feature (when used, Auto Correction is not available). • Instruct subjects that in case of prolonged use of acetaminophen, the temp target feature can be used repeatedly and in succession. • Pump has cybersecurity encryptions to prevent hacking.

• Hypoglycemia
• Severe hypoglycemia
• Hyperglycemia
• Diabetic ketoacidosis
• User entry error
  ○ Patient administering boluses by entering false carb doses leading to hypoglycemia or hyperglycemia
  ○ 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 SmartGuard 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 (SmartGuard)
• Hypoglycemia or hyperglycemia related to entering or exiting Closed Loop (SmartGuard)
• Insulin over-delivery due to potential interference from acetaminophen
• Cyber security hacking into pump	

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. • 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 SG readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the SG 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: • 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 SG readings in order to make diabetes treatment decisions. • Instruct to check their meter glucose if there are any concerns that the SG 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 and glucagon on hand for hypoglycemia.
Risk with Acetaminophen Use	**Prevention and Mitigation**
Potential risks with acetaminophen may include: • False elevation of SG readings potentially resulting in an over-delivery of insulin which may cause hypoglycemia. 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	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 to verify their glucose levels. • If acetaminophen is taken, while the SmartGuard™ feature is active, subjects will be instructed to use the temp target feature (when used, Auto Correction is not available). • Instruct subjects that in case of prolonged use of acetaminophen, the temp target feature can be used repeatedly and in succession.

• Allergic reactions including those which are serious and potentially fatal can occur • Kidney disease • Lowered blood counts (red cells, and white cells)	

10.2 Risk Minimization

Refer to "Prevention and Mitigation" column in the table under **Section 10.1**.

10.3 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.

10.4 Risk-Benefit Rationale

The main benefit of this study is that subjects may experience improved glucose control. Since Fiasp insulin has not been previously studied with the 780G system in all age groups, there is a theoretical risk that the 780G pump's closed loop algorithm may not maintain the same level of glucose control achieved with other insulins although modeling has indicated that use of Fiasp insulin will not result in any clinically significant change in clinical outcomes. Additionally, risk related to the pump delivering too much or not enough insulin are further minimized through a variety of safety checks that are an integral part of the 780G closed loop algorithm.

10.5 Risk Determination (US Only)

In the opinion of the sponsor, this study is considered to be a significant risk (SR) study. Results of an evaluation of the requirements per 21 CFR Part 812.3, led to the SR determination as follows:

- The devices present potential for serious risk to subject health, safety, or welfare.
- The devices are for a use of substantial importance in treating disease, and presents potential for serious risk to subject health, safety, or welfare.

Therefore, submission of an Investigational Device Exemption (IDE) application to the United States FDA is required.

11. Adverse Events

11.1 Adverse Events

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 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, assessment of seriousness, and description that includes the details of the event.

11.2 Definitions and Classification of Adverse Events

Medtronic uses the definitions provided in ISO 14155:2020 and 21 CFR 812 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. 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.[2]

Severe Hyperglycemia is defined as hyperglycemia (BG greater than [>] 300 mg/dL or 16.7 mmol/L) with BG 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: BG 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.[3]

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)

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) foetal distress, foetal 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 Adverse Device Effect (UADE) (21 CFR 812.3(s))

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

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 to entry: 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.

11.3 Reporting of Adverse Events

The investigator or designee will record ALL AEs and DDs while the subject is enrolled in the clinical study (Refer to **Section 13** for DDs reporting).

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 (e.g., needle (blood draw) insertion pain).

Examples of device or procedure related AEs include:

- ***Device*** related (ADE): insertion site infection
- Serious adverse ***device effect***: cellulitis at device insertion site requiring hospitalization
- ***Procedure*** related AE: bruising at needle (blood draw) insertion site

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 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 EOS participation; however, there will be no eCRF entry for the ongoing follow-up.

11.4 Notification of Adverse Events

Sponsor Notification:

The investigational center staff must report all AEs to Medtronic in a timely manner. All severe hypoglycemia, DKA, SAE, SADE, and DD with SADE potential 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 de-identified known details of the event. 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 Medtronic's secure upload application. All source documents/medical records should be redacted of patient identifiers (full name, address, etc.) prior to providing to the sponsor. Each source page should be identified with the subject ID.

11.5 Expedited Safety Reporting Requirements

US only: For device studies, investigators are required to submit a report of a UADE to the sponsor and the reviewing IRB as soon as possible, but in no event later than 10 working days after the investigator first learns of the event (812.150(a)(1)).

US and Canada: The sponsor will notify the investigator and EC/IRB of any event that results in a safety report per regulations to the FDA/Health Canada. Documentation of EC/IRB notification of any safety event must be kept at the investigational center and a copy sent to the sponsor.

It is the responsibility of the investigator to follow their EC/IRB reporting requirements.

11.6 Adverse Event and Device Deficiency Classification

All AEs and DDs will be reviewed by sponsor and will be classified according to the responsibilities as outlined below in **Table 7**.

Upon sponsor's receipt of an event, a Safety representative will review the AE/DD for completeness and accuracy and when necessary will request clarification and/or additional information from the Investigator.

It is the responsibility of the investigator and sponsor to abide by any additional AE reporting requirements stipulated by the IRB/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, UADE/USADE, and DD with SADE potential
Diagnosis	Investigator	Based on presenting signs and symptoms and other supporting data
	Sponsor	MedDRA term assigned based on the data provided by Investigator

11.7 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.

This review would include the subjects' description of the event, study device uploads and medical records (if applicable) from the treating facility. These records will be made available to sponsor.

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:

- **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, 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.

- **Possible:** the relationship with the use of the investigational device, comparator, or the relationship with procedures, 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 where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.

- **Probable**: the relationship with the use of the investigational device, comparator, or the relationship with procedures, seems relevant and/or the event cannot reasonably be explained by another cause.

- **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);
  - 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**

11.8 Anticipated or Unanticipated

If an AE is determined to be related to the study device the sponsor will then assess the event to determine if it is anticipated or unanticipated.

- **Anticipated:** the event is identified in the CIP; labeling; report of priors/ IB or user guide.
- **Unanticipated:** the event has not been previously identified in the CIP; labeling; report of priors/ IB or user guide.

12. Data Review Committees

12.1 Clinical Events Committee

A clinical events committee (CEC) consisting of external physicians with an expertise in endocrinology and the management of diabetes including insulin pumps and CGM will be convened. The CEC will review AEs as required per protocol, which include reports of:

- Serious adverse event
- Serious adverse device effect
- Unanticipated adverse device effect
- Unanticipated serious adverse device effect
- Severe hypoglycemia
- Diabetic ketoacidosis
- Severe hyperglycemia

During the study, the following steps will be taken for:

- Unanticipated adverse device effects (UADE)

- Unanticipated Serious Adverse Device Effects (USADE)
- Device related DKA
- Device related severe hypoglycemia

US Only: Sponsor will notify Food and Drug Administration (FDA) within approximately 72 hours of knowledge of the event and provide updates to those regulatory authorities as information becomes available.

Canada only: Sponsor will notify local regulatory authorities as information becomes available per local requirements.

CEC is to review and adjudicate the event within 10 days from the time that the sponsor is notified.

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 IRBs/ ECs and regulatory authorities, if required.

The CEC may review applicable information for device related AEs which may include:

- Whether or not the event was unanticipated
- Review of sensor data from CareLink Personal/CareLink system software report (when applicable)
- Review of pump data from CareLink Personal/CareLink system software report (when applicable)
- Misuse of the device by the user

Review of events may require the following information. Final disposition may be delayed based on obtaining this information:

- Monitoring by sponsor at investigational center
- Device return and failure analysis
- CareLink Personal/CareLink system software upload and review of software reports
- Subject clarification to investigational center regarding details about the event
- Source documents that support event: Paramedic records; ER records; Lab records; Hospital admission and discharge summary

The following factors should be carefully considered in the CEC's recommendation to sponsor:

1. Was the severe hypoglycemia or DKA related to the AHCL algorithm, or was it related to a known insulin pump risk? For example, a question that may be considered in DKA would be whether the event was related to an infusion set issue or caused by the AHCL algorithm.

2. Another important consideration would be if the severe hypoglycemia, severe hyperglycemia or DKA event was related to a device malfunction versus patient non-compliance. For example, if a software anomaly leading to an under-delivery of insulin is discovered versus the subject repeatedly ignoring alarms prompting the subject to take action.

3. Severe hypoglycemia, severe hyperglycemia or DKA caused directly by an infusion set issue when the study pump is functioning as intended would likely result in acceptance to proceed with the study versus severe hypoglycemia or DKA that are directly caused by the AHCL algorithm or a device malfunction might stop study enrollment or entire study altogether.

4. It should be noted that the final determination of causality related to 780G system that is made by the CEC may include additional factors which the members consider to be clinically relevant and important.

12.2 Data Monitoring Committee

A data monitoring committee (DMC) consisting of external physicians with an expertise in Endocrinology and the management of insulin-requiring diabetes including CGM, along with an external statistician will be convened to review study progress and safety. The Board will convene approximately every 90 days. The Board will also meet when ad hoc review is required.

The DMC will perform 4 main functions:

First: DMC will track and trend the overall safety of the study.
Event rate, defined as number of events per 100 patient years will be reviewed by the DMC with respect to the following:

- Event rate of all SAEs
- Event rate of severe hypoglycemia
- Event rate of severe hyperglycemia
- Event rate of DKA
- Event rate of device related AEs

Second: Based on their meetings, DMC will recommend a decision to the sponsor regarding the following:

- Whether or not enrollment should be halted.
- Whether or not the entire study will need to be stopped including for those subjects who have received study devices already.

Note: If it is decided to withdraw subjects from participation in the study or if the study is stopped, subjects will be followed-up in accordance with standard practice by their own providers.

Third:
During the study, the following steps will be taken for:

- Unanticipated adverse device effects (UADE)
- Unanticipated Serious Adverse Device Effects (USADE)
- Device related DKA
- Device related severe hypoglycemia

DMC is to meet within 10 days from the time that the CEC adjudicates an event as one of the above. If possible, the investigator should be available to answer questions by DMC.

Based on their meeting, DMC will recommend a decision to the sponsor regarding the following:

- Whether or not enrollment should be halted.
- Whether or not the entire study will need to be stopped including for those subjects who have received study devices already.

Note: If it is decided to withdraw subjects from participation in the study or if the study is stopped, subjects will be followed-up in accordance with standard practice by their own providers.

Fourth: The DMC will review Safety data and provide a recommendation to the sponsor regarding staged enrollment of pediatric subjects:
The DMC will provide a recommendation to proceed with the following staged enrollment:

The enrollment of subjects 7-17 years of age will not move forward until 10 subjects 18 years or older have completed 30 days of the study period and the Data Monitoring Committee (DMC) has determined that it is safe for 7-17 year olds to be enrolled into the study.

General guidance for DMC's recommendations to sponsor should be based on the following:

In general, a DMC recommendation regarding study stoppage or resumption of enrollment should be made to the sponsor within 1 week of the DMC meeting where the determination is made. However, if more data is needed, the DMC may meet again to re-assess their decision within 2 weeks or when required data becomes available.

In their recommendation to the sponsor, the DMC may take into account the thresholds listed below for the number of subjects experiencing hypoglycemia requiring assistance from another person or DKA to identify when the number of subjects experiencing these events exceeds the number that would be anticipated for the study population over the duration of this study. These thresholds should be interpreted with caution due to potential differences in study populations and study design.

a. Rates taken from type 1 exchange (Cengiz et. Al, and Weinstock et. Al), are higher than the clinical studies STAR 3, 530G adult in-home study (CEP266) and 530G Pediatric in-home study (CEP287).
b. Reasons for lower rates of severe hypoglycemia and DKA in the clinical studies mentioned could be related to several factors including but not limited to the exclusion of those with DKA or severe hypoglycemia, additional attention secondary to mandatory study visits, selection bias of motivated patients willing to perform study procedures and access to free study devices during the course of the study.
c. The DMC should consider stopping study if rates of severe hypoglycemia and DKA are significantly worse (e.g., higher) in AHCL than rates provided by clinical trials mentioned in **Table 8**.
d. Age consideration may also be factored in by the DMC. For example, severe hypoglycemia rates in those >25 years may be higher than those 25 years and below.
e. Should DKA and/or severe hypoglycemia occur early in the study, the DMC should consider that the higher event rate may not necessarily represent a significant safety concern.

Table 8. Hypoglycemia/ Hyperglycemia/ DKA Threshold

Adverse Event	Reference	Reference Rate > 25 years old	Reference Rate 15-25 years old	Reference Rate <15 years old
Severe Hyperglycemia events per 100 patient years	CER 302	NA	NA	71.64
DKA events per 100 patient years	STAR 3 Bergenstal et. al	SAP arm: 0.68 Control arm: 0	SAP arm: 2.7 Control arm: 3.6	SAP arm: 2.2 Control arm: 0
	530G Adult in-home study CEP 266 (MDT on file)	1.27	3.4	N/A
	Pediatric in-home study CEP 287 (MDT on file)	N/A	N/A	0
	Type 1 exchange Weinstock et. al	4.8	N/A	N/A
	Type 1 exchange Cengiz et. al	N/A	9.9	9.9
Severe hypoglycemia per 100 patient years	STAR 3 Bergenstal et. al	SAP arm: 16.5 Control arm: 20.9	SAP arm: 5.4 Control arm: 3.9	SAP arm: 10.2 Control arm: 3.6
	530G Adult in-home study CEP 266 (MDT on file)	0.85	0	N/A
	530G Pediatric in-home study CEP 287 (MDT on file)	N/A	N/A	1.42
	Type 1 exchange Weinstock et. al	11.8	N/A	N/A
	Type 1 exchange Cengiz et. al	N/A	6.2	6.2

Severe hypoglycemia and DKA event rates were taken from the following:

1. Richard Bergenstal et.al: Effectiveness of Sensor-Augmented Insulin-Pump Therapy in Type 1 Diabetes. New England Journal of Medicine, 2010; 363:311-20

2. Weinstock et. al: Severe hypoglycemia and diabetic ketoacidosis in adults with type 1 diabetes: results from the T1D Exchange clinic registry. J Clin Endocrinol Metab. 2013 Aug;98(8):3411-9.

3. Cengiz et. al: Severe hypoglycemia and diabetic ketoacidosis among youth with type 1 diabetes in the T1D Exchange clinic registry. Pediatr Diabetes. 2013 Sep;14(6):447-54.
4. MDT on file: Statistical Analysis Plan (SAP) for CEP304, 056-F286

13. Device Deficiencies and Troubleshooting

The subjects will be instructed to contact the investigational center staff for questions or concerns regarding study devices.

All DDs reported directly to the investigational center staff by a subject and those experienced by the investigational center staff will be reported on the appropriate eCRF in a timely manner. In addition, an eCRF should also be completed by the investigational center staff for each reported DD that did not lead to an Adverse Event. A DD that results in an AE should be captured on an AE CRF only.

Subjects participating in the study are expected to have mild irritation from device wear at times. Only discomfort occurring at a threshold resulting in early removal of the device should be reported as a DD or adverse event.

Device Deficiency (ISO 14155:2020)
A device deficiency is any inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety, or performance.

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

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

Each DD will be assessed for SADE potential defined as:
A DD 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

To return a study device as part of a DD, the subject is to contact the investigational center staff, and the investigational center staff should then follow the study procedures for returning products with DDs. For a list of study devices that needs to be return to the sponsor, please consult your study materials.

It is the responsibility of the investigator to follow their EC/IRB reporting requirements.

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 on eCRFs, subject questionnaires, 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.

14.2 Subject Disposition

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

14.3 Subject Demographics and Baseline Characteristics

Subject characteristics, including age, gender, race, ethnicity, medical diagnosis, height, weight, BMI, and baseline HbA1c will be summarized by descriptive statistics (mean, standard deviation, minimum, median, and maximum) for continuous variables and by counts and percentages for categorical variables.

[redacted]

14.5 Endpoints and Hypotheses

Safety and effectiveness endpoints will be evaluated independently for ages 18-80 and ages 7-17.

14.5.1 Primary Safety Endpoint

Age 18-80:

- The overall mean change in HbA1c, $\Delta\mu_{780G}$, from baseline to end of 3-month study period will be estimated and compared by a non-inferiority test to the threshold of -0.50% with a margin of 0.4%. A significance level of 0.025 (one-sided) will be used. Analysis will be performed on the ITT and PP populations.

  The hypothesis of non-inferiority is mathematically expressed as:

  H_0: $\Delta\mu_{780G} \geq -0.50\% + 0.4\%$

  H_a: $\Delta\mu_{780G} < -0.50\% + 0.4\%$

Age 7-17:

- The overall mean change in HbA1c, $\Delta\mu_{780G}$, from baseline to end of 3-month study period will be estimated and compared by a non-inferiority test to the threshold of -0.38% with a margin of

0.4%. A significance level of 0.025 (one-sided) will be used. Analysis will be performed on the ITT and PP populations.

The hypothesis of non-inferiority is mathematically expressed as:

H_0: $\Delta\mu_{780G} \geq -0.38\% + 0.4\%$

H_a: $\Delta\mu_{780G} < -0.38\% + 0.4\%$

14.5.2 **Analysis of Effectiveness Endpoint**

14.5.2.1 Primary Effectiveness Endpoint

Age 18-80:

- The mean % of time, μ_{780G}, in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared by a non-inferiority test to the threshold of 73.7% with a margin of 7.5%. A significance level of 0.025 (one-sided) will be used. The 7.5%, which is approximately 100 minutes increase in TIR per day, was also observed from the HCL pivotal trials. It is loosely correlated to ~0.5% reduction in A1c as well. Analysis will be performed on the ITT and PP populations.

  The hypothesis of non-inferiority is mathematically expressed as:

  H_0: $\mu_{780G} \leq 73.7\% - 7.5\%$

  H_a: $\mu_{780G} > 73.7\% - 7.5\%$

Age 7-17:

- The mean % of time, μ_{780G}, in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared by a non-inferiority test to the threshold of 65.3% with a margin of 7.5%. A significance level of 0.025 (one-sided) will be used. The 7.5%, which is approximately 100 minutes increase in TIR per day, was also observed from the HCL pivotal trials. It is loosely correlated to ~0.5% reduction in A1c as well. Analysis will be performed on the ITT and PP populations.

  The hypothesis of non-inferiority is mathematically expressed as:

  H_0: $\mu_{780G} \leq 65.3\% - 7.5\%$

  H_a: $\mu_{780G} > 65.3\% - 7.5\%$

Pass/Fail Criteria:
The study pass/fail criteria is based on statistical hypothesis of the primary endpoints. The study for each age cohort (age 18-80 and age 7-17) will be considered as success when the evaluation criteria of both primary safety and effective endpoints meets the predefined threshold per cohort.

Justification for Exclusion of Particular Information from the testing of the Hypothesis:
Not Applicable.

14.5.2.2 Analysis of Secondary Effectiveness Endpoints

Age 18-80:

- Secondary Effectiveness Endpoint: The mean % time, μ_{780G}, in hypoglycemia (< 54 mg/dL [3.0 mmol/L]) will be estimated and compared by a non-inferiority test to the threshold of 0.86% with a margin of 2%. A significance level of 0.025 (one-sided) will be used. Analysis will be performed on the ITT and PP populations. The 2% came from not more than 30 minutes increase in hypoglycemia per day to establish a non-inferiority test.

  The hypothesis of non-inferiority is mathematically expressed as:

  H_0: $\mu_{780G} \geq 0.86\% + 2\%$

  H_a: $\mu_{780G} < 0.86\% + 2\%$

- Secondary Effectiveness Endpoint: The mean % of time, μ_{780G}, in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared by a simple superiority test with a significance level of 0.025 (one-sided). Analysis will be performed on the ITT and PP populations.

  The hypothesis of superiority is mathematically expressed as:

  H_0: $\mu_{780G} \leq 73.7\%$

  H_a: $\mu_{780G} > 73.7\%$

Age 7-17:

- Secondary Effectiveness Endpoint: The mean % time, μ_{780G}, in hypoglycemia (< 54 mg/dL [3.0 mmol/L]) will be estimated and compared by a non-inferiority test to the threshold of 0.71%

with a margin of 2%. A significance level of 0.025 (one-sided) will be used. The 2% came from not more than 30 minutes increase in hypoglycemia per day to establish a non-inferiority test. Analysis will be performed on the ITT and PP populations.

The hypothesis of non-inferiority is mathematically expressed as:

H_0: $\mu_{780G} \geq 0.71\% + 2\%$

H_a: $\mu_{780G} < 0.71\% + 2\%$

- Secondary Effectiveness Endpoint: The mean % of time, μ_{780G}, in range (TIR 70-180 mg/dL [3.9 -10.0 mmol/L]) will be estimated and compared by a simple superiority test with a significance level of 0.025 (one-sided). Analysis will be performed on the ITT and PP populations.

The hypothesis of superiority is mathematically expressed as:

H_0: $\mu_{780G} \leq 65.3\%$

H_a: $\mu_{780G} > 65.3\%$

[redacted]

[redacted]

14.5.4 **Safety Data Summarized**

Serious Adverse Events (SAE)

Serious Adverse Device Effects (SADE)

Unanticipated Adverse Device Effects

- Unanticipated Serious Adverse Device Effect

Incidence of Severe Hypoglycemia

Incidence of Severe Hyperglycemia

Incidence of DKA

14.5.5 **Device Deficiencies**

Descriptive summary will be used to characterize DDs:

- All reports of device issues.

[redacted]

[redacted]

[redacted]

- [redacted]

  [redacted]

- [redacted]

  [redacted]

- [redacted]

  [redacted]

- [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

14.7 Final Reports

The study results will be summarized and presented in the final report.

15. Ethics

15.1 Statement(s) of Compliance

This study will be conducted in compliance with international ethical and scientific quality standards, known as Good Clinical Practice (GCP). GCP includes review and approval by an independent EC/IRB before initiating a study, continuing review of an ongoing study by an EC/IRB, and obtaining and documenting the freely given informed consent of a subject before initiating the study.

The CIP336 was designed to reflect the GCP principles outlined in ISO 14155:2020 and other international clinical requirements outlined below. These include the protection of the rights, safety and well-being of human subjects, controls to ensure the scientific conduct and credibility of the clinical investigation and the definition of responsibilities of the sponsor and investigators. In accordance with ISO 14155:2020, the sponsor shall avoid improper influence on, or inducement of, the subject, monitor, any investigator(s) or other parties participating in, or contributing to, the clinical investigation. All investigators shall avoid improper influence on or inducement of the subject, sponsor, monitor, other investigator(s) or other parties participating in or contributing to the clinical investigation. AE and DD handling in the CIP336 is ISO 14155:2020 compliant for all participating geographies.,

The principles of the Declaration of Helsinki (DoH) have been implemented through the IC process, EC approval, study training, clinical trial registration, pre-clinical testing, risk-benefit assessment and publication policy.

Ultimately, all study sites in all geographies will follow and comply with:

- Principles of DoH
- 21 CFR Part 11 (Electronic Records, Electronic Signatures)
- 21 CFR Part 54 (Financial Disclosure by Clinical Investigators)
- The CTA
- The procedures described within this CIP
- Local EC Requirements

In addition to the regulatory requirements outlined above, the study will be conducted according to federal, national and local laws, regulations, standards, and requirements of the countries/geographies where the study is being conducted. These include but are not limited to:

- In the United States, the study will be conducted under an FDA IDE in compliance with 21 CFR Parts:
  - 50: Protection of Human Subjects
  - 54: Financial Disclosure by Clinical Investigators
  - 56: IRBs
  - 812: IDEs
- In Canada, SOR/98-282, Section 59-88 will be followed and Mandatory Problem Reporting 59(1), 59(2), 60 (1)).

The study will be publicly registered prior to in accordance with the 2007 Food and Drug Administration Amendments Act (FDAAA) and DoH on http://clinicaltrials.gov (PL 110-85, section 810(a)). In addition, the study may be registered in local regulatory databases where required by local law.

Approval of the CIP and CIP amendments is required from the following groups prior to any study procedures at a study site:

- Medtronic
- Geography-specific regulatory authorities (if regulatory approval is required)
- An independent medical EC or IRB.

Similarly, approval of subsequent revisions to the CIP is required at each study site from the above mentioned groups prior to implementation of the revised CIP at the investigational center.

15.2 Role of the Sponsor's Representatives

Sponsor representatives may provide support as required for the study, such as technical support at investigational center. Sponsor representatives may provide technical support as required for the study under supervision of the PI, including:

1) Provide study training relevant and pertinent to the involvement of personnel conducting study activities and investigator responsibilities.
2) Technical support will be provided during study period.
3) Technical support will be under the supervision of a study investigator, but no data entry on the eCRF shall be performed by Medtronic personnel or their representatives at investigational centers.
4) Technical support to conduct device interrogations.

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.

15.3 Investigator's Responsibilities

Per 21 CFR 56.102, an investigator means "an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject) or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team."

Per ISO14155:2020, an investigator means "individual member of the investigation site team designated and supervised by the PI at an investigation site to perform critical clinical-investigation-related procedures or to make important clinical-investigation related decisions."

Each investigational center shall designate a primary investigator who will have overall responsibility for the conduct of the investigation at the investigational center.

The primary investigators (and co-investigators if applicable) are responsible for conducting the study in accordance with this CIP, CTA, 21 CFR Part 812 that apply to significant risk (SR) device studies/ ISO14155:2020, applicable regulations, and any conditions of approval imposed by the reviewing EC/IRB or regulatory authority requirements. The investigator's responsibilities include but are not limited to:

- Conduct of investigation in accordance to draft guidance from FDA, "Protecting the Rights, Safety, and Welfare of Study Subjects - Supervisory Responsibilities of Investigators"/ International guidelines for clinical trials on medical devices ISO 14155:2020, to meet responsibilities with respect to protect human subjects and ensuring the integrity of the data from clinical investigations. This guidance is also intended to clarify FDA's/ regulatory authority's expectations concerning the investigator's responsibility:

    1) to supervise a clinical study in which some study tasks are delegated to employees or colleagues of the investigator or other third parties, and
    2) 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
- 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/assent are met in accordance with 21 CFR 50/ ISO 14155:2020
- Supervising the use of investigational device. An investigator shall permit an investigational device to be used only with subjects under the investigator's supervision. An investigator shall not supply an investigational device to any person not authorized to receive it.
- 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:
  - attribution, legibility, and timeliness of source data
  - all relevant correspondence with another investigator, an EC/IRB, the sponsor, a monitor, or FDA/regulatory authority, including required reports
  - records of receipt, use or disposition of study devices
  - records of each subject's case history and exposure to the device, including information reported in the eCRFs and in all other required reports
  - the CIP, with documents showing the dates of and reasons for each deviation from the CIP

  - any other records the FDA/ regulatory authority requires to be maintained by regulations or by specific requirement for a category of investigations or a particular investigation

- Preparation and submission to Medtronic and, when required, FDA/ regulatory authority and the reviewing EC/IRB, the following complete, accurate, and timely reports:
  - any reportable AEs (see **Section 11)** occurring during an investigation
  - progress reports on the investigation as required by the FDA/ regulatory authority and EC/IRB
  - 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/assent
  - any further information requested by the FDA/ regulatory authority and EC/IRB about any aspect of the investigation
- Permitting FDA or other 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.

16. Study Administration

16.1 Training of Clinical Staff

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 on the Delegation of Authority Log. Training may contain both lecture and hands-on experience.

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

16.2 Monitoring

Monitoring visits may be conducted at the start, during and at the closure of the clinical study in accordance with Medtronic SOPs and the Monitoring Plan. At minimum, it will be verified whether signed and dated ICF/assent form have been obtained from each subject at the point of enrollment and that AEs discussed in **Section 11** were reported via completion of the AE eCRFs. More details regarding the monitoring activities (frequency of monitoring visits, planned extent of source data verification) are described in the Monitoring Plan.

16.2.1 Accessibility of Investigational Center Staff and Study Materials

The PI(s), his/her delegate(s) and the study coordinator(s) shall be accessible to Medtronic field personnel, monitor, regulatory authority personnel, and the Clinical Study Manager. This accessibility is of particular importance for reviewing data in the eCRF. Access to subject's medical files for source data verification will need to be granted prior to any monitoring visits.

16.2.2 Audits and Investigational Center Inspections

In addition to regular monitoring visits, the sponsor may conduct 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. 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 sponsor 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/IRB review, and regulatory inspections.

16.2.3 Investigational Center Disqualification

Sponsor and/or the EC/IRB retain the right to disqualify an investigational center and remove all study materials at any time. Specific instances that may precipitate investigational center disqualification include but are not limited to:

- Unsatisfactory subject enrollment with regards to quantity.

- Persistent non-compliance to protocol procedures on the part of an investigator/investigational center
- Inaccurate, incomplete, and/or untimely data recording on a recurrent basis.
- The incidence and/or severity of adverse experiences in this or other studies indicating a potential health hazard caused by the device.
- Unsatisfactory accountability of investigational devices.

A written statement fully documenting the reasons for such a termination will be provided to sponsor, the EC/IRB, investigational center(s) and other regulatory authorities, as required.

16.3 Data Management

16.3.1 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 the 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 File. The EDC 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 to the use of the eCRFs. Access to final eCRFs for study conduct will be granted after training is performed and prior to patient's enrollment.

16.3.2 CareLink Personal/CareLink System Software

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 Personal/CareLink system software by the investigator or designated investigational center staff and subjects at home. The system uses TLS technology, which encrypts all data it stores (21 CFR Part 11 compliant). The data in the different databases are linked to each other via the subject's ID.

16.3.3 Patient Questionnaires

The questionnaires will be provided in local language in the countries. Subjects will be provided a link to complete the questionnaires online. Refer to CIP336 Questionnaire Guide. If the online link cannot be accessed due to technical problems, subjects will complete the questionnaire using a paper format. The investigator, or designated investigational center staff, will then enter the subject's responses from the paper questionnaires to online once it becomes available. If paper format is used, the investigator or designated investigational center staff should maintain the original paper source in the subject's source file.

16.3.4 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 the reportable AEs (see **Section 11**). After data entry, eCRFs should be submitted (i.e., saved) so that monitors can proceed with data verification without delay.

16.3.5 Data Review and Processing

Data management will be done according to sponsor 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.

16.4 Direct Access to Source Data/Documents

The subject's clinic file, CareLink Personal/CareLink system software data, laboratory reports, questionnaires 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.

16.5 Confidentiality

The investigator will ensure that the subject's anonymity is maintained. Subjects will not be identified in any publicly released reports of this study. All records will be kept confidential to the extent provided by federal, state and local law. 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. 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 locked and all computer entry and networking programs will be done with coded numbers only.

16.6 Liability and Subject Compensation

The subjects may receive compensation for participation in this study. Travel fees to the site may be reimbursed for study specific visits if required by local regulations. Refer to the ICF for details of the subject's compensation, if applicable.

16.6.1 Insurance (Canada)

Medtronic Canada ULC is a wholly owned subsidiary of Medtronic, which as the parent company of such entity maintains appropriate general liability insurance coverage as required under applicable laws and regulations and will comply with applicable local law and custom concerning specific insurance coverage. If required, a General Liability insurance statement/certificate will be provided to the EC.

16.7 CIP Amendments

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

Sponsor can decide to review the CIP based on new information, or for other reasons, and will submit any significant amendment to the CIP, including a justification for this amendment, to the appropriate regulatory authority (if applicable) for their approval and to the investigators to obtain approval from their EC/IRB. The investigator will only implement the amendment after the sponsor has obtained regulatory authority (if applicable) approval and the amendment has been approved by the EC/IRB. Administrative amendments to the CIP will be submitted to the EC/IRB for notification.

16.8 Investigational Center Compensation

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

16.9 Records and Reports

16.9.1 Investigator Records

At a minimum, the following records must be kept by the investigator:

- All essential study documents and correspondence that pertains to the clinical study
- CIP and, if applicable, any amendments
- IB/report of prior investigations and/or user guide
- Medtronic and EC/IRB-approved Subject ICF/assent form
- EC/IRB and regulatory authority approval or notification
- Fully signed clinical study agreements (i.e., including Investigator Statement and Signature Page, Clinical Trial Agreement and Confidential Disclosure Agreement)
- Completed Delegation of Authority Log
- Training documentation of all investigational center staff
- Subject Screening log and/or subject ID log
- Signed, dated and fully executed Subject ICF/assent form
- Source documentation
- Fully executed eCRFs and corrections
- Report of AEs and DDs
- Device accountability records
- CIP Deviation/ CIP Non-Compliance, if any
- Clinical Bulletins (if applicable)- A brief official update or summary of current study news on a matter of immediate interest and high importance to investigational center surrounding the CIP.
- Current signed and dated CV of PI (and key study team members if required per local requirements)
- Study reports

16.9.2 Investigator Reporting Responsibilities

Table 9. Investigator Reporting Requirements Applicable to the US

Report	Submit to	Description/Constraints
AEs and DDs	Sponsor, IRB, and regulatory authority, where applicable	Refer to **Section 11** and 13 for reporting requirements.

Report	Submit to	Description/Constraints
Withdrawal of IRB approval (either suspension or termination)	Sponsor	An investigator shall report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.
Progress report	Sponsor and IRB	The investigator must submit this report to the sponsor and IRB at regular intervals but in no event less than yearly.
Study deviations	Sponsor and IRB	Notice of deviations from the CIP to protect the life or physical wellbeing of a subject in an emergency shall be given as soon as possible but no later than 5 working days after the emergency occurred.
Failure to obtain informed consent/assent prior to investigational device use	Sponsor and IRBs	If an investigator uses a device without obtaining informed consent/assent the investigator shall report such use within 5 working days after device use.
Final report	Sponsor IRBs Relevant Authorities	This report must be submitted within 3 months of study completion or termination of the investigation or the investigator's part of the investigation.
Other	Sponsor, IRB and FDA	An investigator shall, upon request by a reviewing IRB, FDA or any other regulatory authority, provide accurate, complete, and current information about any aspect of the investigation.

Table 10. Investigator Reporting Requirements Applicable to Canada

Report	Submit to	Description/Constraints
AEs and DDs	Sponsor, EC, and regulatory authority, where applicable	Refer to **Section 11** and 13 for reporting requirements.
Incident(s) as described in Section 59 of SOR/98-282	EC Sponsor, manufacturer and importer of the device	The investigator must report the incident(s) as described in Section 59 of SOR/98-282 and the circumstances surrounding it within 72 hours after it comes to his/her attention, per Section 81(k)(v).

Report	Submit to	Description/Constraints
Withdrawal of EC approval	Sponsor and Relevant Authorities	The investigator must report a withdrawal of approval by the reviewing EC of the investigator's part of the investigation within 5 working days.
Study Deviations	Sponsor and EC	Notice of deviations from the CIP to protect the life or physical well-being of a subject in an emergency shall be given as soon as possible, but no later than 5 working days after the emergency occurred.
Final Report	IRBs/ECs and Relevant Authorities	This report must be submitted within 3 months of study completion or termination.

16.10 Record Retention

The sponsor and investigator will retain all records and documents pertaining to this study. 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. These records are to be retained in a secure storage facility maintained by the investigational center until 2 years (or longer if local laws require) after approval of the above-listed study devices or termination of the study, whichever is longer. The investigator should not dispose of these records without the approval of the sponsor.

16.11 Suspension or Early Termination

Sponsor or a 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 or because of a business decision). If the clinical study is terminated prematurely or suspended, sponsor shall promptly inform the investigators and regulatory authorities (if applicable) of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform the reviewing EC/IRB and the study subjects.

16.11.1 Early Investigational Center Suspension or Termination

Sponsor, EC/IRB or a regulatory authority may decide to suspend or prematurely terminate an investigational center (e.g., in case of expiring approval of the reviewing EC/IRB, non-compliance to the CIP, or lack of enrollment). Suspended clinical studies cannot be resumed without permission from EC/IRB and regulatory authority (if applicable). If an investigational center is suspended or prematurely terminated, sponsor shall promptly inform the investigator(s) of the termination or suspension and the

reason(s) for this. The investigator shall then promptly inform the reviewing EC/IRB and the study subjects.

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/IRB, if applicable.

16.11.2 Subject Follow-Up In Case of Termination

In case of early investigational center suspension or termination, all subjects should be contacted to plan an early termination visit 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. Following suspension or early termination, subjects will receive standard medical care from their own providers.

16.12 Study Close-Out

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

16.13 Publication and Use of Information

Publications from this CIP will be handled according to SOPs and as indicated in the CTA. A separate Publication Plan will describe the publication strategy and processes for publications of the study. Clinical trials data will be shared by Medtronic with its manufacturer (Novo Nordisk) of the insulin used in the study.

Publications will adhere to authorship criteria defined by the International Committee of Medical Journal Editors (ICMJE, Uniform requirements for manuscripts submitted to biomedical journals, www.icmje.org). Individual authorship criteria defined by the target journal or conference will be followed when it differs from ICMJE criteria.

Authors, including Medtronic personnel, must at a minimum meet all of the conditions below:

- Substantial contributions to conception and design of the work, or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND

- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Decisions regarding authorship and contributor-ship will be made by a publication planning committee. The selected authors will be responsible for drafting the publication. All selected authors must fulfill the authorship conditions stated above to be listed as authors, and all contributors who fulfill the conditions must be listed as authors.

All investigators not listed as co-authors will be acknowledged as the "Medtronic CIP336 Study Investigators" and will be individually listed according to the guidelines of the applicable scientific journal when possible and affiliation. Any other contributors will be acknowledged by name with their specific contribution indicated.

Publications from the study will be handled according to Medtronic Global Standard Operating Procedures and as indicated in the Clinical Trial Agreement. 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 prior to subject enrollment. Study results, when available, will be posted in this database.

17. References

1. Beato-Víbora PI, Gallego-Gamero F, Lázaro-Martín L, Romero-Pérez MDM, Arroyo-Díez FJ. Prospective Analysis of the Impact of Commercialized Hybrid Closed-Loop System on Glycemic Control, Glycemic Variability, and Patient-Related Outcomes in Children and Adults: A Focus on Superiority over Predictive Low-Glucose Suspend Technology. *Diabetes Technology and Therapeutics.* 2020;22(12):912-919.
2. Cryer PE. Defining and reporting hypoglycemia in diabetes: A report from the American diabetes association workgroup on hypoglycemia. *Diabetes Care.* 2005;28(5):1245-1249.
3. Hyperglycemic Crises in Diabetes. *Diabetes Care.* 2004;27(SUPPL. 1):S94-S102.

18. Appendices

18.1 Names and addresses

18.1.1 Investigational Centers and EC/IRB

The names and addresses of investigators and participating investigational centers will be kept under separate cover.

18.1.2 Monitor(s) Contact Information

The study will be monitored by the Medtronic Clinical& Regulatory Solutions (MCRS) Global Monitoring and monitoring duties to be entrusted under:

[redacted]
Medtronic
710 Medtronic Parkway
Minneapolis, MN 55432

The names and addresses of monitors will be kept under separate cover.

18.1.3 Clinical Laboratory(ies) Contact Information

The names and addresses of clinical laboratory(ies) will be kept under separate cover. The most current list of the contact persons is available upon request.

18.2 Labeling of Devices

The current labels for investigational devices and IFUs for all devices will be provided to the investigators under separate cover.

18.3 Sample Consent Materials

Samples of the following consent forms/materials will be provided in a separate cover which includes the California Experimental Subject's Bill of Rights (if applicable), ICF, assent form, and the HIPAA Authorization.

18.4 Questionnaires

The questionnaires are available in local language and will be provided under a separate cover upon request 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.1	Not Applicable, New Document	Not Applicable, New Document	Not Applicable, New Document	Not Applicable, New Document	[redacted]
A.2	• See "Attachment 1: CIP336 Description of Protocol Changes Version A.1 to A.2" for details on changes • Updated Medtronic Extended infusion set model number for Canada; harmonized throughout CIP, as applicable in title page, synopsis, device regulatory status table, and DA Table • Updated Study Design section • Updated Background section • Updated Table 1 – Canada Device Regulatory Status on the Medtronic Extended infusion sets • Updated Table 4- Canada DA Requirements for Medtronic infusion set • Updated Study Site Activation section • Updated Schedule of Events section • Updated Table 6, Visit Details • Updated End of Subject Participation in Study section	See "Attachment 1: CIP336 Description of Protocol Changes Version A.1 to A.2" for details		ICFs, CRFs, and PFF	[redacted]

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
	• Updated Definitions and Classification of Adverse Events section • Updated Insurance sections for Canada and Europe				

A.3	• See "Attachment 1: CIP336 Description of Protocol Changes Version A.2 to A.3" for details on changes
	• Added new simulation data analysis
	• Updated Table 1 – Europe Device Regulatory Status on the apps and Blue Adapter
	• Updated Table 6, Visit Details
	  ○ Conversion for mmol/L added for 100 mg/dL Auto Basal target settings
	  ○ Added "x" mark at Visit 6,7, and 8 for "Print and review CareLink Reports"
	  ○ Removed investigational center staff to "collect" questionnaires as this will be direct entry
	• Updated Recording Data section
	• Updated Patient Questionnaires section
		See "Attachment 1: CIP336 Description of Protocol Changes Version A.2 to A.3" for details		None	[redacted]

A.4	• See "Attachment 1: CIP336 Description of Protocol Changes Version A.3 to A.4" for details on changes • Updated Glossary	See "Attachment 1: CIP336 Description of Protocol Changes Version A.3 to A.4" for details		ICFs, CRFs, and PFF	[redacted]

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

	• Updated List of Trademarks
	• Removed Precision Xtra ketone meter and updated to generic term, ketone meter
	• Updated Background section
	• Updated Study Design section
	  ○ Removed statement about enrollment of 2-6 years old not taking place in Europe.
	  ○ Added instructions for parents/caregivers/companions should be in same residence or building overnight as their child
	  ○ Added use of push notifications for hypoglycemia alarms when pediatric subjects are away from parents/caregivers
	  ○ Modified to ensure use of the 120 mg/dL (6.7 mmol/L) setpoint during the run-in period Setpoints have been arranged to allow for titration during the first part of the study period. Meal and exercise challenges will take place during weeks 2 and 4 of the study period, at each setpoint.
	  ○ Added a checklist to document subject/parent/caregiver training				

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
	and materials will be provided to them on important information to be used during the study. ○ Added meal and stress challenges to evaluate system with insulin under investigation at different Auto Basal target setpoints. ○ Added an additional enrollment stage to monitor different age groups as they use the system with a new insulin. All meal and exercise challenges are taking place during the first 28 days of the study period. • Harmonized term used across CIP "caretaker" to "caregiver" • Clarified that subjects and parents/caregivers on how to use glucose and glucagon, in addition to having glucose and glucagon on hand for hypoglycemia (Updated in Study Design and Visit Details Table) • Separated pediatric groups by enrollment target • Inclusion criteria ○ #2c- Updated for 2-6 years of age from "a clinical diagnosis of type 1				

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
	diabetes for 3 months or more" to "a clinical diagnosis of type 1 diabetes for 6 months or more" ○ #4- harmonized term of caretaker to parent/caregiver ○ #6,7,12 and #13- administrative updates ○ New inclusion criteria #14- add subjects must be willing take Fiasp insulin in study period • Updated Study Visit Schedule, Figure, and Visit Details-Updated to 14 study visits. The visits were updated to account for subject training needs after starting on the 780G system. • Corrected conversion of mg/dL to mmol/L, as applicable • Updated title of Table 2 • Descriptive endpoints added to capture the inclusion of meal and exercise challenges • Canada Device Regulatory Status for Extended infusion set updated to investigational • Europe Device Regulatory Status for Guardian 4 Sensor and Guardian 4 Transmitter updated				

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

	• Extended infusion set for Device Accountability Requirements Table updated for Canada
	• Updated Blue Adapter description section
	• Updated Schedule of Events section
	• Updated Investigator/Investigational Center Selection and Medical Staff section
	• Updated Table 6, Visit Details
	  ○ Additional study procedures to align with new study requirements
	  ○ Added "Adjust pump settings"
	  ○ Added "Ask subjects if they require assistance, e.g., additional training"
	  ○ Added "Instruct subjects and their parents/caregivers on diabetes self-management principles, including the use of glucose and glucagon in the event of severe hypoglycemia" "
	  ○ Added "Instruct/Remind subjects about the requirement to perform a meal challenge during the run-in period. SmartGuard should not be activated"
	  ○ Added "Instruct/Remind subjects about the requirement to perform meal and exercise challenges during				

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
	the study period" • Updated Box to "secure upload application" throughout CIP • Updated Subject Consent section • Updated Calibration of CGM Risk section • Updated Recording Data and Patient questions section to address back up plan in case the link to a panned electronic questionnaire is not available • Updated End of Subject Participation in Study/ Completion of Study section • Updated Table 12 on reporting of Study Deviations • Updated prevention and mitigation for Risks with Insulin Administration and Pumps • Updated Severe Hyperglycemia and SAE definition • Updated Notification of Adverse Events section • Updated Expedited Safety Reporting Requirements section • Updated DMC section to align with staged enrollment • Updated Statement(s) of Compliance section • Updated Publication and Use of Information section				

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
	• Updated References section				
A.5	• Updated IDE number • Added "standard of care in Europe" for ketone meter description • Updated Study Design section • Updated staged enrollment for both Stage 1 and Stage 2- 28 days completion to 30 days • Updated number of subject enrollment (numbers in pediatric and adult age group revised) and number of subject entering study period • Updated Study Visit Schedule and Figure for Visit 3, 4, and 8 • Updated Visit Details Table (column title)- For Visit 3,4, and 8- added asterisk "Required for subjects without CGM or closed loop experience; as needed for all others." • Added parents/caregivers/companions, where applicable throughout CIP • Updated Blood Ketone Values section • Updated Table 7- Added that parent(s)/guardian(s)/companion(s) "should be present at night with subjects" to align with updated study design • Updated Sample Size Considerations/Sample	See "Attachment 1: CIP336 Description of Protocol Changes Version A.4 to A.5" for details		ICFs, CRFs, Home Reference Guide, and CIP336 Questionnaire Guide	[redacted]

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
	Size Justification section • Updated Expected Drop-out Rates				
A.6	• Added Guardian 4 Sensor model number for Canada (MMT-7040C4) • Updated Statistical Analysis for Endpoints and Hypothesis • Updated Analysis Populations and Handling of Missing Data, Error section • Updated Pass/Fail Criteria	See "Attachment 1: CIP336 Description of Protocol Changes Version A.5 to A.6" for details		PFF	[redacted]
A (Equivalent to FDA Version A.7)	• Updated to train "companions" on diabetes management principles, check blood ketones, check SMBG, and all parts of device system. A checklist will be implemented and completed for the companions as well. The changes are reflected throughout CIP, as applicable, and under the following sections: ○ Study Design ○ Study Visit Schedule ○ Visit Details Table • Updated prevention and mitigation for Risks with Insulin Administration and Pumps- added parent/caregivers and companions should be present during meal and exercise challenges	See "Attachment 1: CIP336 Description of Protocol Changes Version A.6 to A.7" for details		ICFs	[redacted]
B (Equivalent	• See "Attachment 1: CIP336 Description of Protocol Changes Version A to B.1" for	See "Attachment 1: CIP336 Description of Protocol		IB and Product Management	[redacted]

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
to FDA Version B.1)	details on changes • Updated year in copyright statement • Updated Medtronic Extended infusion set model numbers for all regions and harmonized throughout CIP, as applicable in title page, synopsis, device regulatory status table, and DA Table • Updated Study Design section • Updated Exclusion Criteria #12 • Updated Fiasp insulin accountability at subject level (DA Requirements Table for all regions) • Updated Return or Disposal of Study Devices section • Updated Schedule of Events and HbA1c section- typo corrected from Visit 5 to Visit 7. • Updated Study Stopping Rules section • Updated prevention and mitigation for the following (added "and glucagon"): Risks with Insulin Administration and Pumps and Risk with Closed Loop Therapy • Updated Clinical Events Committee section • Updated Data Monitoring Committee section	Changes Version A to B.1" for details		Assessment Form	[redacted]
C.1	• See "Attachment 1: CIP336 Description of Protocol Changes Version B to C.1" for details	See "Attachment 1: CIP336 Description of Protocol		ICF, CIP Training PPT, Device Training	[redacted]

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
	on changes • Transferred protocol to the revised Enterprise Clinical QMS CIP template (056-F275, Version D) • Added Health Canada ITA number • Added FootPrint™ to list of trademarks • Updated Glossary section • Clarified kit numbers and added pump numbers for Europe • Clarified kit number and added meter number for Canada • Updated Synopsis (Clinical Study Type), Objective, and Background section: Harmonized term "efficacy" to "effectiveness" • Clarified the use of SmartGuard during Run-in Period and Study Period for both subjects with Auto Mode and without Auto Mode experience. The changes are reflected under the following sections: o Study Design o Visit Details Table • Updated Study Design & Visit Details Table- changed setting requirements for more flexibility per investigator's discretion • Updated Study Design section- clarified the role of the FoodPrint™ phone app in the collection	Changes Version B to C.1" for details		PPT, CRF Requirements, CCGs, Product Management Assessment Form, Pump Training Checklist, Instructions for Site, Device Tasks by Visit, Questionnaire Guide, Questionnaire Flow Chart, Visit Calculator, and Source Worksheets	[redacted]

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
	of data during meal and exercise challenges • Removed enrollment of subjects 2-6 years of age. The changes are reflected under the following sections: ○ Study Design ○ Sample Size/Study Population ○ Inclusion Criteria ○ Rationale ○ Data Monitoring Committee ○ Synopsis and Endpoints for following subheader sections: Primary Safety Endpoint, Primary Effectiveness Endpoint, and Secondary Effectiveness Endpoints ○ Endpoints and Hypotheses ○ Primary Safety Endpoint, Primary Effectiveness Endpoint, and Secondary Effectiveness Endpoints ○ Sample Size Considerations/Sample Size Justification • Removed device training requirements for companions. The changes are reflected under the following sections: ○ Study Design ○ Study Visit Schedule ○ Visit Details Table ○ Potential Risks				

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

	• Updated inclusion criteria #8- expanded criteria to specify that subjects have a maximum total daily dose of 250 units or less
	• Added new visit under Study Period – Day 44 (±3 days) after Visit 7. The changes are reflected under the following sections:
	  ○ Study Design
	  ○ Study Visit Schedule
	  ○ Visit Schedule figure
	  ○ Visit Details Table
	• Typo for setpoint at Visit 10 corrected in Study Visit Schedule
	• Table 1- Updated the following device regulatory status for:
	  ○ EU on pump, sensor, and transmitter
	  ○ Canada on Medtronic Extended Reservoir
	• Table 2- estimated numbers of Medtronic Extended Infusion set updated (updated both item description and units per subject)
	• Updated MiniMed 780G Insulin Pump section
	• Table 3- Updated US DA Requirements for Smartphone
	• Table 4- Updated Canada DA Requirements for Smartphone
	• Table 5- Added asterisk next to study pump to denote kit distribution				

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
	• DA requirements table for all regions - Added asterisk next to study meter to denote kit distribution • Updated Subject Enrollment section • Updated prevention and mitigation for the Risks with Insulin Administration and Pumps, associated with hypoglycemia- added "and glucagon" • Updated Data Monitoring Committee section • Updated Descriptive Endpoints section • Updated Analysis Populations and Handling of Missing Data, Error section for PP population • Updated Investigational Centers and EC/IRB section				
C (Equivalent to Version C.2)	• See "Attachment 1: CIP336 Description of Protocol Changes Version C.1 to C.2" for details on changes • Corrected trademark for FootPrint™ • Updated attribution statement in copyright statement • Transferred protocol to the revised Enterprise Clinical QMS CIP template (056-F275, Version E) • Updated Study Design section- Active Insulin Time settings updated during the run-in period and the first 3 weeks of study period	See "Attachment 1: CIP336 Description of Protocol Changes Version C.1 to C.2" for details		Pump Training Checklist	[redacted]

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.1	• See "Attachment 1: CIP336 Description of CIP Changes Version C to D.1 " for details on changes • Updated year in copyright statement • Added Australia as local sponsor • Removed all Europe information, associated study and regulatory requirements related to Europe as reflected under the following: ○ Title page ○ Glossary section ○ Synopsis section ○ Study Design section ○ Background section ○ Table 1 ○ Table 2 ○ Product Accountability section ○ Study Population section ○ Visit Details Table ○ Subject Consent section ○ Unplanned CIP Deviations section ○ Reporting Requirements for Study Deviations section ○ Table 6 ○ Reporting of Adverse Events section ○ Expedited Safety Reporting Requirements section	See "Attachment 1: CIP336 Description of CIP Changes Version C to D.1 " for details		ICF, CIP Training PPT, Device Training PPT, CRF Requirements, CCGs, DRGs, Site materials, and Subject facing materials	[redacted]

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
	○ Adverse Event and Device Deficiency Classification section ○ Clinical Events Committee section ○ Statement(s) of Compliance section ○ Insurance (Europe) section ○ Table 12 (removed) ○ Investigational Centers and EC/IRB section • Updated the following details under Study Design section: ○ regular sized meal challenge with missed meal bolus ○ subjects to avoid additional meal/snack or exercise up to four hours after the start of the challenge ○ removed the word "live" training • Updated "weeks" with associated study visit • Harmonized start of Auto Basal target at 120 mg/dL, 100 mg/dL, and investigator's discretion as specified under Study Design for the following: ○ Study Visit Schedule section ○ Visit Details Table • Increased study duration and number of investigational centers • Added Exclusion Criteria for 780G users and				

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
	harmonized updates to Study Design section and Visit Details Table • Updated Schedule of Events Section- removed exceptions for Telemedicine • Updated Table 1: ○ US regulatory classification for Medtronic Extended reservoir updated to non-investigational ○ For ketone meter and Fiasp, added "N/A" under "MDT Model number/ part number" column • Visit Details table- additional "As needed" updated for "Dispense Fiasp" on subsequent office visits • Updated Publication and Use of Information section • Updated Monitor(s) Contact Information section				
D (Equivalent to Version D.2)	• See "Attachment 1: CIP336 Description of CIP Changes Version D.1 to D.2 " for details on changes • Updated Study Design section	See "Attachment 1: CIP336 Description of CIP Changes Version D.1 to D.2" for details		ICF, Training materials, Site materials, and Subject facing materials	[redacted]
E (Equivalent to Version	• See "Attachment 1: CIP336 Description of CIP Changes Version D to E" for details on changes • Updated Glossary section	See "Attachment 1: CIP336 Description of CIP Changes Version D to E" for details		Product Management Assessment Form,	[redacted]

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.1)	• Updated Canada model numbers and device regulatory status for Medtronic Extended infusion set under the following: ○ Title page ○ Synopsis section ○ Table 1 with footnote for commercial stock disbursement after depletion of investigational Extended infusion sets stock products ○ Table 4 • Updated Table 1: ○ Updated US Device Regulatory Status for Guardian 4 Sensor (MMT-7040) and Guardian 4 Transmitter (MMT-7841) ○ Added footnote for commercial stock disbursement after depletion of sensor and transmitter investigational stock products. ○ Updated Canada Regulatory Status for the following: ▪ Medtronic CareLink Personal software ▪ Medtronic CareLink system software ▪ MiniMed Clinical App			ICFs, Training materials, Site materials, and Subject facing materials	

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
	▪ CareLink Clinical App • Updated Background section • Added the MiniMed Mobile App under as reflected under the following: ○ Title page ○ Synopsis section ○ Study Design section ○ Table 1 ○ MiniMed 780G Insulin Pump section ○ Figure 1 ○ Accessory Applications – 780G system section ○ Blue Adapter section ○ Table 5 ○ Recording Data section • Updated use of SmartGuard is not allowed during challenges in the run-in period as reflected under the following: ○ Synopsis section ○ Study Design section ○ Table 5 • Updated name of MC2 to MCRS • Updated Labeling of Devices section				