| Medtronic | |
|---|---|
| **Study Title** | IMPACT2: In-Home Study with MiniMedTM 780G Pump Automated Control in Type 2 – Evaluation of the AHCL System in Adults with Insulin-requiring Type 2 Diabetes |
| **NCT Number** | NCT05238142 |
| **Document Description** | Clinical Investigation Plan (Version F) |
| **Document Date** | 08-APR-2024 |

| Medtronic<br>**Clinical Investigation Plan** | |
|---|---|
| **Clinical Investigation Plan (CIP) Study Title** | **IMPACT2**: **I**n-Home Study with **M**iniMed™ 780G **P**ump **A**utomated **C**ontrol in **T**ype **2** - Evaluation of the AHCL System in Adults with Insulin-requiring Type 2 Diabetes |
| **CIP Identifier** | 341 |
| **Investigational Device Exemption (IDE) Number** | G210352 |
| **Study Product Names & Model Numbers** | **Investigational Product**<br>• MiniMed™ 780G Insulin Pump (MMT-1884) - referred to as the study pump throughout this protocol<br>• MiniMed™ 780G BLE 2.0 Insulin Pump (MMT-1884) - referred to as the study pump throughout this protocol<br>• Guardian™ 4 Glucose Sensor (MMT-7040) - referred to as the study sensor throughout this protocol<br>• Guardian™ 4 Transmitter (MMT-7841)<br>• Disposable Sensor (MMT-5100) – labeled as DS5 referred to as study sensor throughout this protocol<br><br>**Non-Investigational Product**<br>• Medtronic Extended infusion set (MMT-430, MMT-431, MMT-432, MMT-433, MMT-440, MMT-441, MMT-442, MMT-433 and MMT-443) or other approved Medtronic infusion sets<br>• Medtronic Extended Reservoir (MMT-342) or other approved Medtronic reservoirs<br>• One-Press Serter (MMT-7512) - referred to as the Serter throughout this protocol<br>• Transmitter Charger (MMT-7715)<br>• Tester (MMT-7736L)<br>• Medtronic CareLink™ Personal software (MMT-7333)<br>• Medtronic CareLink™ system software (MMT-7350)<br>• Roche Accu-Chek™ Guide Link Glucose Meter (08116083022, 09651926001M, 09651942001M) -referred to as the Accu-Chek Guide Link study meter throughout this protocol<br>• MiniMed Clinical App (MMT-6103 Android™ app; MMT-6104 IOS™ app)<br>• MiniMed Mobile App (MMT-6101 Android™ app; MMT-6102 IOS™ app)<br>• CareLink Clinical App (MMT-6113 Android™ app; MMT-6114 IOS™ app) |

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| | • Blue Bluetooth® Low Energy Adapter (ACC-1003911)- referred to as the Blue Adapter in this protocol<br>• Ketone meter to be used for blood ketone measurements only<br>• Accu-Chek Guide test strips (07453736001)<br>• Sponsor-provided smartphone for subject and/or site use, upon request<br>• Sponsor-provided tablet for site use, upon request |
| **Description of CIP** | This study will confirm the safety and effectiveness of the MiniMed™ 780G system in adults with insulin-requiring type 2 diabetes. |
| **Sponsor** | Medtronic MiniMed<br>("Medtronic")<br>18000 Devonshire St<br>Northridge, CA 91325<br>866.948.6633 |
| **Document Version** | F (Equivalent to FDA Version F.1) |
| **Version Date** | 08-APR-2024 |
| **Document Reference Number** | D00591227 |



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# Table of Contents

# 1. Glossary

| Abbreviations | |
|---|---|
| ADE | Adverse Device Effect |
| AID | Automatic Insulin Delivery |
| 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 |
| CTA | Clinical Trial Agreement |
| CV | Curriculum Vitae |
| DD | Device Deficiency |
| DKA | Diabetic Ketoacidosis |
| DMC | Data Monitoring Committee |
| DoH | Declaration of Helsinki |
| eCRF | Electronic Case Report Form |
| EDC | Electronic Data Capture |
| EOS | End of Study |
| ER | Emergency Room |
| FDA | Food and Drug Administration |
| GAD | Glutamic Acid Decarboxylase |
| GCP | Good Clinical Practice |
| HbA1c | Glycosylated hemoglobin |
| HIPAA | Health Insurance Portability and Accountability Act |
| HHS | Hyperglycemic Hyperosmolar Syndrome |
| ICF | Informed Consent Form |
| ID | Identification |
| IDE | Investigational Device Exemption |
| IEC | Independent Ethic Committee |
| IFU | Instructions for Use |
| IRB | Institutional Review Board |
| ISO | International Organization for Standardization |
| IV | Intravenous |
| MCRS | Medtronic Clinical & Regulatory Solutions |
| MDI | Multiple Daily Injections |
| NGSP | National Glycohemoglobin Standardization Program |
| PC | Personal Computer |

| Abbreviations | |
|---|---|
| PI | Principal Investigator |
| PP | Per Protocol |
| QC | Quality Control |
| SADE | Serious Adverse Device Effect |
| SAE | Serious Adverse Event |
| SAP | Sensor Augmented Pump |
| SG | Sensor Glucose |
| SGLT | Sodium-glucose Linked Transporter |
| 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 |
| TS | Technical Support |
| TSH | Thyroid-stimulating hormone |
| UADE | Unanticipated Adverse Device Effect |

# 2. Synopsis

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|---|---|
| **Title** | **IMPACT2**: **I**n-Home Study with **M**iniMed™ 780G **P**ump **A**utomated **C**ontrol in **T**ype **2** – Evaluation of the AHCL System in Adults with Insulin-Requiring Type 2 Diabetes |
| **Clinical Study Type** | Safety and Effectiveness Evaluation |
| **Sponsor** | Medtronic MiniMed, Inc.<br>("Medtronic")<br>18000 Devonshire St<br>Northridge, CA 91325<br>866.948.6633 |
| **Indication Under Investigation** | Use of the MiniMed™ 780G system by adults with insulin-requiring type 2 diabetes. |
| **Study Product Names & Model Numbers** | **Investigational Product**<br>• MiniMed™ 780G Insulin Pump (MMT-1884) – referred to as the study pump throughout this protocol<br>• MiniMed™ 780G BLE 2.0 Insulin Pump (MMT-1884) – referred to as the study pump throughout this protocol<br>• Guardian™ 4 Glucose Sensor (MMT-7040) – referred to as the study sensor throughout this protocol<br>• Guardian™ 4 Transmitter (MMT-7841)<br>• Disposable Sensor (MMT-5100) – labeled as DS5 and referred to as study sensor throughout this protocol<br><br>**Non-Investigational Product**<br>• Medtronic Extended infusion set (MMT-430, MMT-431, MMT-432, MMT-433, MMT-440, MMT-441, MMT-442, and MMT-443) or other approved Medtronic infusion sets<br>• Medtronic Extended Reservoir (MMT-342) or other approved Medtronic reservoirs<br>• One-Press Serter (MMT-7512) – referred to as the Serter throughout this protocol<br>• Transmitter Charger (MMT-7715)<br>• Tester (MMT-7736L)<br>• Medtronic CareLink™ Personal software (MMT-7333) device<br>• Medtronic CareLink™ system software (MMT-7350)<br>• Roche Accu-Chek™ Guide Link Glucose Meter (08116083022, 09651926001M, 09651942001M) – referred to as the Accu-Chek Guide Link study meter throughout this protocol<br>• MiniMed Clinical App (MMT-6103 Android™ app; MMT-6104 IOS™ app)<br>• MiniMed Mobile App (MMT-6101 Android™ app; MMT-6102 IOS™ app)<br>• CareLink Clinical App (MMT-6113 Android™ app; MMT-6114 IOS™ app) |

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|---|---|
| | • Blue Bluetooth® Low Energy Adapter (ACC-1003911)- referred to as the Blue Adapter in this protocol<br>• Ketone meter, to be used for blood ketone measurements only<br>• Accu-Chek Guide test strips (07453736001)<br>• Sponsor-provided smartphone for subject and/or site use, upon request<br>• Sponsor-provided tablet for site use, upon request |
| **Purpose** | The purpose of this study is to confirm the safety and effectiveness of the MiniMed™ 780G system in adult patients with insulin-requiring type 2 diabetes in a home setting, which will support a future regulatory submission for labeling expansion. |
| **Objective(s)** | The objective of this study is to assess the safety and effectiveness of the MiniMed 780G system when used by adults with insulin-requiring type 2 diabetes. |
| **Study Design** | This study is a multi-center, single arm study in adult subjects with insulin-requiring type 2 diabetes, conducted in 2 phases. Phase 1 has been completed. Subjects who participated in Phase 1 have been transitioned to Phase 2, if they consented to do so. New subjects will only participate in Phase 2.<br><br>**Phase 1: MiniMed™ 780G insulin pump with Guardian 4 Sensor**<br>Phase 1 studied the MiniMed™ 780G insulin pump with Guardian 4 Sensor. See **Section 18.4.1** (Completed Study Design in **Appendix 4: Phase 1**) for the Study Design for Phase 1. This phase is now complete.<br><br>**Phase 2: MiniMed™ 780G BLE 2.0 insulin pump with Disposable Sensor 5 (DS5)**<br>Phase 2 will study the MiniMed™ 780G BLE 2.0 insulin pump with the disposable sensor DS5. The combined run-in period and study period will be approximately 135 days long.<br><br>The period from Visit 1 (consent and screening) through Visit 8 should be completed within 45 days.<br><br>**Run-in Period (Visits 2-8):**<br><br>The run-in period begins at Visit 2 and ends once Visit 9 occurs.<br><br>The intent of the run-in period will be to allow subjects to become familiar with new study devices, while using their own insulin, Humalog™ (insulin lispro injection), NovoLog®/NovoRapid® (insulin aspart solution for injection), or Admelog (insulin lispro injection).<br><br>During the run-in period of the study, subjects will be using the study pump in Manual Mode, with only the Sensor Augmented Pump (SAP) function activated (i.e., |

SmartGuard™ feature turned OFF). The "Suspend before Low" and "Suspend on Low" features may be used.

| Therapy at Screening | Pump Setting During Run-in Period |
|---|---|
| Continuous Subcutaneous Insulin Infusion (CSII) | Manual Mode |
| SAP (no closed loop) | Manual Mode |
| SAP with closed loop (i.e., Automatic Insulin Delivery (AID) in non-Medtronic pump | Manual Mode |
| SAP (with closed loop) in Medtronic pump as Auto Mode | SmartGuard feature with Auto Correction OFF |

All subjects will be trained on diabetes management principles, such as the treatment of hyperglycemia and hypoglycemia. In addition, there will be training by investigational center staff regarding the need to have access to and how to use glucose and glucagon in case of hypoglycemia.

Companions/care partners will be instructed that they should be with the subject in the same residence or building complex overnight.

If the MiniMed Clinical/MiniMed Mobile app and the CareLink Clinical app are being used companions/care partners 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 work, other activities. Instructions on the appropriate operation of the apps will be provided.

For study purposes, subjects will be instructed to perform self-monitoring of blood glucose (SMBG) if they are experiencing a severe hypoglycemic event, severe hyperglycemic event, hyperglycemic hyperosmolar syndrome (HHS) or diabetic ketoacidosis (DKA).

- Blood ketones will be measured by all subjects using a ketone meter when:
  - the subject is symptomatic for high blood glucose or
  - the sensor glucose is >300mg/dL, the BG should be checked by fingerstick and, if BG is >300mg/dL, blood ketones should be checked

As a precaution, subjects 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

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| | therapy during the study or experience study device issues (e.g., infusion set occlusion with high glucose).<br><br>Subjects will be instructed to insert study sensors only in the locations that are specified in the User Guide. Subjects should be reminded about appropriate study sensor placement at each office visit. Information about predominant location of study sensor insertions will be collected on an electronic case report form (eCRF) at the end of a subject's participation.<br><br>Subjects will be trained on all parts of the device system. Companions/care partners should be trained on how to respond to high or low glucose events. This should involve training conducted by investigational center staff. A training checklist for each subject should be completed by investigational center-based trainers. Companions/care partners should be available for relevant parts or, if desired, all of this training, either in person or virtually.<br><br>After completion of training on the study devices, subjects will be asked to attend additional visits in the days immediately following the start of system use, as needed. They may also take advantage of having continued access to the digital learning content, provided it is available at study start.<br><br>**Study Period (Visits 9-18):**<br>The study period begins at Visit 9 and ends at the conclusion of Visit 18.<br><br>Subjects will continue using the study pump and study sensor and will use the SmartGuard feature for approximately 90 days during the study period. Subjects should use the system with the SmartGuard feature (with Auto Correction ON) turned on at all times. When prompted by the pump, subjects should take appropriate measures and follow directions on the pump to remain in, or return to, SmartGuard. During times when subjects are not able to use SmartGuard, they should use the system in Manual Mode (e.g., using Suspend before low and Suspend on low settings).<br><br>**Pump Settings:**<br>During the first 3 weeks (between Visits 9 and 14) of the study period, a 120 mg/dL 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 at the investigator's discretion.<br><br>During the next 3 weeks (between Visits 14 and 16) of the study period, a 100 mg/dL Auto Basal Target should be set. Active Insulin time is recommended to be set to 2-3 hours or at investigator's discretion. |

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| | During the remaining weeks (any time after Visit 16) 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 discretion.<br><br>The Auto Basal target setting and Active Insulin Time should be set as shown above unless there is a documented safety reason that would not permit these settings to be used.<br><br>After completion of training on SmartGuard functions, subjects 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 digital learning content, provided it is available at study start.<br><br>**SMBG recommendations for 780G BLE 2.0 system:**<br>With the 780G BLE 2.0 system and the study sensor, calibration is not required. However, a calibration is optional, and it will automatically 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 SmartGuard. 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).<br><br>**Companions:**<br>Subjects will be required to have a companion (may be care partner) who resides (or will live) in the same building (or home) during the study at night. Companions should be able to check SMBG, give glucose and/or administer glucagon. |
| **Sample Size and Investigational Centers** | A total of up to 575 subjects, with at least 300 subjects entering the study period of Phase 2, with insulin-requiring type 2 diabetes age 18-80 will be enrolled at up to 40 investigational centers across the United States.<br><br>To widen the distribution of the type 2 diabetes population, investigational centers are encouraged to enroll a study population that represents a wide variety of races, ethnicities, BMI, TDD of insulin, and background diabetes medications. |
| **Duration** | The study is anticipated to last approximately 36 months from first investigational center initiation to study period completion. Individual subject participation is expected to be approximately 135 days through the study period of each phase. |
| **Inclusion Criteria** | 1. Is age 18 – 80 years at time of screening.<br>2. Has a clinical diagnosis of type 2 diabetes for 2 years or more as determined via medical record or source documentation by an individual qualified to make a medical diagnosis.<br>3. Is on multiple daily injection (MDI) regimen (basal/bolus regimen with long-acting insulin and rapid-acting analogs), defined as greater than or equal to 2 injections per day for at least 3 months prior signing the informed consent, or |

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| | CSII pump therapy with or without CGM. The investigators will use their discretion to verify that insulin requirements have been stable for the last 3 months prior to screening.<br>4. Is able to comply with technology, according to Investigator's judgment<br>5. Does not require a legally authorized representative to consent on their behalf due to mental or intellectual disability.<br>6. Is willing to perform fingerstick blood glucose measurements as needed.<br>7. Is willing to wear the system continuously throughout the study.<br>8. Has a Glycosylated hemoglobin (HbA1c) of less than 10% (as processed by Central Lab) at time of screening visit.<br>**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.<br>9. 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.<br>10. 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.<br>11. Is willing to take one of the following insulins and can financially support the use of insulin preparations as required by the study:<br>a) Humalog (insulin lispro injection)<br>b) NovoLog/NovoRapid (insulin aspart injection)<br>c) Admelog (insulin lispro injection) |
| **Exclusion Criteria** | 1. Has a history of 2 or more episodes of severe hypoglycemia, which resulted in any the following during the 6 months prior to screening:<br>a. Medical assistance (i.e., Paramedics, Emergency Room [ER] or Hospitalization)<br>b. Coma<br>c. Seizures<br>2. Has been hospitalized or has visited the ER in the 6 months prior to screening resulting in a primary diagnosis of uncontrolled diabetes.<br>3. Has had diabetic ketoacidosis (DKA) or hyperglycemic hyperosmolar syndrome (HHS) in the last 6 months prior to screening visit.<br>4. Will not tolerate tape adhesive in the area of sensor placement as assessed by a qualified individual.<br>5. Has any unresolved adverse skin condition in the area of sensor placement (e.g., psoriasis, dermatitis herpetiformis, rash, Staphylococcus infection) at time of screening.<br>6. Has (Total Daily Dose) of less than 8 units or greater than 250 units at time of screening.<br>7. Has positive GAD (Glutamic Acid Decarboxylase) Antibody test<br>8. Is female of child-bearing potential and result of pregnancy test is positive at screening |

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| | 9. Is sexually active female of child-bearing potential and is not using a form of contraception deemed reliable by the investigator.<br>10. Is female and plans to become pregnant during the course of the study.<br>11. Is being treated for hyperthyroidism at time of screening.<br>12. Has diagnosis of adrenal insufficiency at time of screening.<br>13. 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.<br>**Note:** Intra-articular injections to treat pain (e.g., joint pain, bursitis, etc.) are permitted<br>14. Is using hydroxyurea at time of screening or plans to use it during the study.<br>15. 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 prior to screening (**Note:** Did not apply to subjects who transitioned from Phase 1 to Phase 2).<br>16. Is currently abusing illicit drugs.<br>17. Is currently abusing marijuana.<br>18. Is currently abusing prescription drugs.<br>19. Is currently abusing alcohol.<br>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.<br>21. Has elective surgery planned that requires general anesthesia during the course of the study.<br>22. Has sickle cell disease, hemoglobinopathy; or has received red blood cell transfusion or erythropoietin within 3 months prior to time of screening.<br>23. Plans to receive red blood cell transfusion or erythropoietin over the course of study participation.<br>24. Is diagnosed with current eating disorder such as anorexia or bulimia.<br>25. Has been diagnosed with chronic kidney disease greater than CKD2 that results in chronic anemia.<br>26. Has a hematocrit that is below the normal reference range of lab used.<br>27. Is on dialysis.<br>28. Has serum creatinine of >2 mg/dL.<br>29. Has celiac disease that is not adequately treated as determined by the investigator.<br>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.<br>31. Has had any of the following cardiovascular events 1 year or more prior to 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. |

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| | Subject may be enrolled if clearance from a board-certified cardiologist is provided prior to or at Screening.<br>32. Is a member of the research staff involved with the study.<br>33. Has used a MiniMed 780G pump prior to screening (**Note:** In Phase 2, this applies to new subjects only). |
| **Study Visit Schedule** | Subjects may participate in 2 phases:<br><br>**Phase 1 (Completed):** Subjects participated in a minimum of 18 planned study visits, as presented in **Section 18.4.3** , for approximately 135 days of device wear. Subjects were allowed to enter a continued access period, following the end of the study period. Phase 1 has been completed. For detailed information, see **Section 18.4 Appendix 4: Phase 1**.<br><br>**Phase 2:** Subjects will participate in a minimum of 18 planned study visits, as presented below in **Synopsis Figure 1**, for approximately 135 days of device wear.<br><br>Virtual office visit (audio visual) may be performed for office visits in cases where an office visit is not possible.<br><br>**Subjects who transitioned from Phase 1 to Phase 2:**<br>Phase 1 subjects were given the opportunity to transition into Phase 2 upon completion of the Phase 1 study period or at a subsequent continued access period visit. Transitioning subjects were expected to complete all required Visit 1 – Phase 2 activities prior to entering Visit 9 – Phase 2 and did not need to complete Visit 2 through Visit 8 of Phase 2.<br><br>**Phase 2: MiniMed™ 780G BLE 2.0 insulin pump with Disposable Sensor 5 (DS5)**<br><br>**Visit 1 to Visit 8 should be completed within 45 days.**<br>• Visit 1 (Office): Consent and screening<br>  ○ Collect labs<br><br>**Run-In Period:**<br>• Visit 2 (Office): Start Run-In<br>  ○ Eligibility has been confirmed<br>  ○ Start study pump and CGM in Manual Mode<br>  ○ Register and upload study pump in CareLink Personal and CareLink system<br>  ○ Ask subjects about adverse events and device performance<br>• Visit 3 (Phone): Day 1 after Visit 2<br>  ○ Ask subjects if they require assistance, e.g., additional training<br>  ○ Ask subjects about adverse events and device performance |

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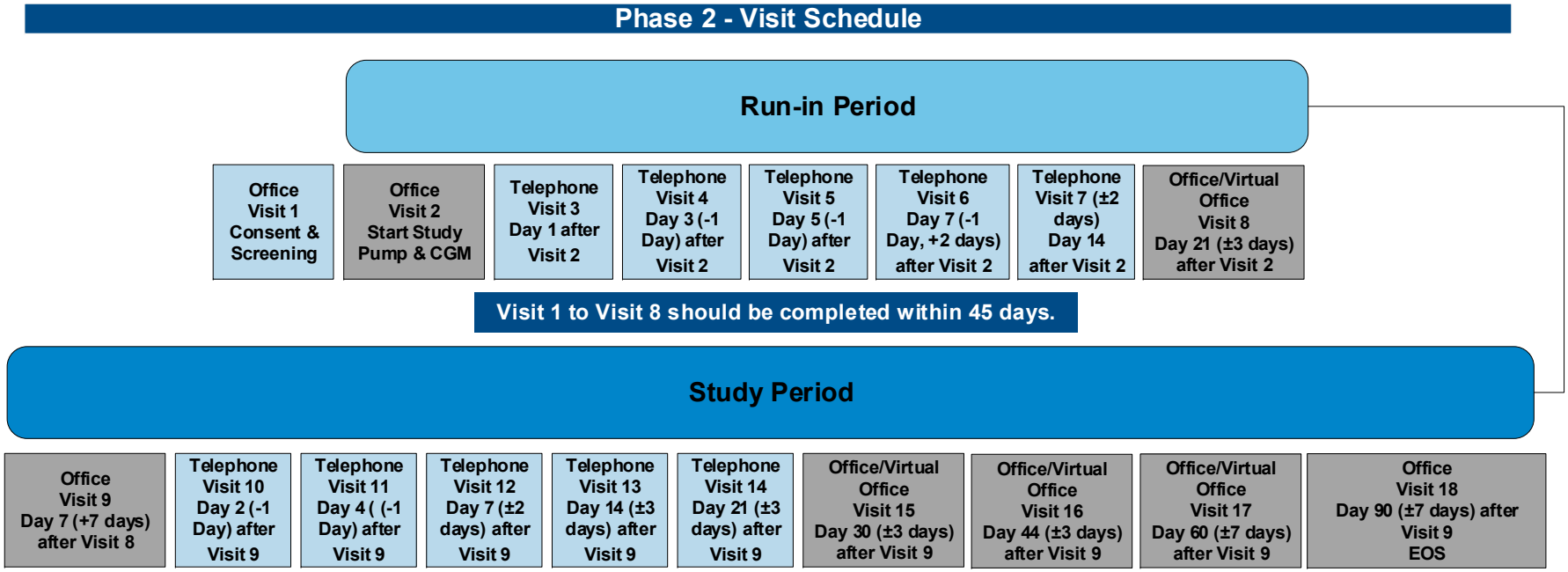
| | ○ Review CareLink reports<br>• Visit 4 (Phone): Day 3 (-1 day) after Visit 2<br>○ Ask subjects if they require assistance, e.g., additional training<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>• Visit 5 (Phone): Day 5 (-1 day) after Visit 2<br>○ Ask subjects if they require assistance, e.g., additional training<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>• Visit 6 (Phone): Day 7 (-1 day, +2 days) after Visit 2<br>○ Ask subjects if they require assistance, e.g., additional training<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>• Visit 7 (Phone): Day 14 (±2 days) after Visit 2<br>○ Ask subjects if they require assistance, e.g., additional training<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>• Visit 8 (Office/Virtual Office): Day 21 (±3 days) after Visit 2<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br><br>**Study Period:**<br>• Visit 9 (Office): Start Study Period, Day 7 (+7 days) after Visit 8<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>○ Start subjects on SmartGuard<br>○ Start auto basal target at 120 mg/dL setpoint<br>• Visit 10 (Phone): Day 2 (-1 day) after Visit 9<br>○ Adjust pump settings as needed<br>○ Ask subjects if they require assistance, e.g., additional training<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>• Visit 11 (Phone): Day 4 (-1 day) after Visit 9<br>○ Adjust pump settings as needed<br>○ Ask subjects if they require assistance, e.g., additional training<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>• Visit 12 (Phone): Day 7 (±2 days) after Visit 9<br>○ Adjust pump settings as needed<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>• Visit 13 (Phone): Day 14 (±3 days) after Visit 9<br>○ Adjust pump settings as needed<br>○ Ask subjects about adverse events and device performance |

| | |
|---|---|
| | ○ Review CareLink reports<br>• Visit 14 (Phone): Day 21 (±3 days) after Visit 9<br>○ Adjust pump settings as needed<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>○ Change auto basal target at 100 mg/dL setpoint and<br>• Visit 15 (Office/Virtual Office): Day 30 (±3 days) after Visit 9<br>○ Adjust pump settings as needed<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>• Visit 16 (Office/Virtual Office): Day 44 (±3 days) after Visit 9<br>○ Adjust Auto Basal target with Active Insulin Time at investigator's discretion<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>• Visit 17 (Office/Virtual Office): Day 60 (±7 days) after Visit 9<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>• Visit 18 (Office): Day 90 (±7 days) after Visit 9<br>○ Collect HbA1C<br>○ Ask subjects about adverse events and device performance<br>○ Review CareLink reports<br>○ Return study devices – unless subject decides to enter continued access period<br>○ End of Study (EOS) – unless subject decides to enter continued access period |

**Synopsis Figure 1. Phase 2 Visit Schedule**




**Note:** Phase 1 subjects were given the opportunity to transition to Phase 2 upon completion of Phase 1 – Study Period or at a subsequent continued access period visit. Phase 1 is now complete and the Phase 1 visit schedule is presented **Section 18.4.2** for reference.

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|---|---|
| **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 by subjects and/or investigational centers calling the 24-Hour Technical Support (TS) for device troubleshooting and device complaints. For additional information, see **Section 13**. |
| **Statistical Analysis for Endpoints and Hypothesis** | The following endpoints will be evaluated for each of the phases, separately.<br><br>**Phase 1:** MiniMed™ 780G insulin pump with Guardian 4 Sensor<br>**Phase 2:** MiniMed™ 780G BLE 2.0 insulin pump with DS5<br><br>**Study Period**<br><br>**Primary Safety Endpoint**<br>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% in reducing HbA1c from baseline to end of 3-month study period. (**Note:** Phase 1 subjects transitioned into Phase 2 will not be included in this analysis for Phase 2.)<br><br>**Primary Effectiveness Endpoint**<br>The mean % of time in range (TIR 70-180 mg/dL) will be estimated and compared to a threshold of 70% by a non-inferiority test with a margin of 7.5% and a significance level of 0.025 (one-sided).<br><br>**Secondary Effectiveness Endpoint**<br>The mean % of time in range (TIR 70-180 mg/dL) will be estimated and compared to a threshold of 70% by a simple superiority test and a significance level of 0.025 (one-sided).<br><br>  |

**Device Deficiencies**

Descriptive summary will be used to characterize device deficiencies:

- All reports of device issues.

**Subject Feedback**

Descriptive summary will be used to characterize study questionnaire results. Refer to CIP341 Questionnaire Guide for administration details.

**Safety Data Summarized**

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

**Run-in Period**

**Device Deficiencies**

Descriptive summary will be used to characterize device deficiencies:

- All reports of device issues.

**Subject Feedback**

Descriptive summary will be used to characterize study questionnaire results. Refer to CIP341 Questionnaire Guide for administration details.

**Safety Data Summarized**

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

**Continued Access Period**

Only applicable for Phase 1.

**Device Deficiencies**

Descriptive summary will be used to characterize device deficiencies:

- All reports of device issues.

**Safety Data Summarized**

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

[redacted]

| | |
|---|---|
| | [redacted] |
| **Study Reports** | **Phase 1**: A study report will be generated once the subjects have completed the continued access period. Primary, secondary, and descriptive endpoints, subject feedback, and safety data for subjects will be summarized and presented in the report.<br><br>**Phase 2**: A study report will be generated once the subjects have completed the study period. Primary, secondary, and descriptive endpoints, subject feedback, and safety data for subjects will be summarized and presented in the report. |

# 3. Introduction

## 3.1 Background

Type 2 diabetes mellitus, formerly known as non-insulin dependent diabetes and mature-onset diabetes, is characterized by a lack of insulin (reduced secretion that can reach an absolute lack) or insulin resistance (reduced insulin sensitivity of insulin receptors in cell membranes). In adults, type 2 diabetes accounts for 90–95% of all diagnosed cases of diabetes.[1] The exact cause of type 2 diabetes remains unknown, although both genetics (race/ethnicity, family history of diabetes, history of gestational diabetes, impaired glucose metabolism) and environmental factors (obesity and lack of exercise) appear to play roles. [2, 3] Type 2 diabetes usually begins as insulin resistance, a disorder in which the cells do not use insulin properly. The pancreas initially responds by increasing insulin production but over time this excess production cannot be maintained, leading to a decrease in insulin production and a lack of insulin.

Algorithm driven closed-loop systems enable automated subcutaneous delivery of insulin in response to real-time continuous glucose sensor readings. Prior Medtronic studies to date have assessed the safety and effectiveness of closed-loop insulin delivery in patients with type 1 diabetes. For some patients with type 2 diabetes whose treatment consists of diet or non-insulin glucose-lowering medications, an episode of severe illness could result in elevated glucose levels that may make it necessary to provide insulin in order to improve and optimize glucose control. Other type 2 patients are using pumps, but do not yet have access to the benefits of closed loop control. Medtronic has conducted a study of pump systems in Type 2 patients, which found that Insulin Pump therapy has a sustained, durable, effect on glycemic control in uncontrolled type 2 diabetes.[4]

The MiniMed 780G system is an advanced hybrid 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 Europe, Australia, and the United States. Previous clinical investigations involved the 670G Version 4.0 pump (contains the 780G AHCL (Advanced Hybrid Closed Loop) algorithm) used in combination with the Guardian Sensor (3) glucose sensor, Guardian Link (3) transmitter, and Humalog or NovoLog. The MiniMed 780G insulin pump has also been used in combination with Guardian 4 glucose sensor and Guardian 4 transmitter.

This investigation is intended to confirm safety and effectiveness of the MiniMed 780G system in patients with type 2 diabetes. The study began with investigation of the MiniMed 780G system with the Guardian 4 Sensor/Transmitter in the type 2 diabetes population. The introduction of the 780G BLE 2.0 system with disposable sensor DS5 into the study is intended to confirm safety and effectiveness of the 780G insulin pump used in combination with the DS5; the DS5 combines the glucose sensor and transmitter into one disposable device. Additional details for non-clinical/clinical testing are provided in the report of prior investigations.

### 3.2 Purpose

The purpose of this study is to confirm the safety and effectiveness of the MiniMed 780G system in type 2 adults in a home setting, which will support a future regulatory submission for labeling expansion.

# 4. Objectives and Endpoints

## 4.1 Objective

The objective of this study is to assess the safety and effectiveness of the MiniMed 780G system when used by adults with insulin-requiring type 2 diabetes.

## 4.2 Endpoints

The following endpoints will be evaluated for each of the phases, separately.

**Phase 1:** MiniMed™ 780G insulin pump with Guardian 4 Sensor

**Phase 2:** MiniMed™ 780G BLE 2.0 insulin pump with DS5

### 4.2.1 During Study Period

#### 4.2.1.1 Primary Safety Endpoint

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% in reducing HbA1c from baseline to end of 3-month study period. (**Note:** Phase 1 subjects transitioned into Phase 2 will not be included in this analysis for Phase 2.)

#### 4.2.1.2 Primary Effectiveness Endpoint

The mean % of time in range (TIR 70-180 mg/dL) will be estimated and compared to a threshold of 70% by a non-inferiority test with a margin of 7.5% and a significance level of 0.025 (one-sided).

#### 4.2.1.3 Secondary Effectiveness Endpoint

The mean % of time in range (TIR 70-180 mg/dL) will be estimated and compared to a threshold of 70% by a simple superiority test and a significance level of 0.025 (one-sided).

#### 4.2.1.5 Device Deficiencies

Descriptive summary will be used to characterize device deficiencies:

- All reports of device issues.

#### 4.2.1.6 Subject Feedback

Descriptive summary will be used to characterize study questionnaire results. Refer to CIP341 Questionnaire Guide for administration details.

#### 4.2.1.7 Safety Data Summarized

- Serious Adverse Events (SAE)
- Serious Adverse Device Effects (SADE)
- Unanticipated Adverse Device Effects (UADE)
- Incidence of Severe Hypoglycemia

- Incidence of Severe Hyperglycemia
- Incidence of DKA
- Incidence of HHS

### 4.2.2 During Run-in Period

#### 4.2.2.1 Device Deficiencies

Descriptive summary will be used to characterize device deficiencies:

- All reports of device issues.

#### 4.2.2.2 Subject Feedback

Descriptive summary will be used to characterize study questionnaire results. Refer to CIP341 Questionnaire Guide for administration details.

#### 4.2.2.3 Safety Data Summarized

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

### 4.2.3 Continued Access Period

Only applicable for Phase 1.

#### 4.2.3.1 Device Deficiencies

Descriptive summary will be used to characterize device deficiencies:

- All reports of device issues.

#### 4.2.3.2 Safety Data Summarized

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

[redacted]

# 5. Study Design

This study is a multi-center, single arm study in adult subjects with insulin-requiring type 2 diabetes, conducted in 2 phases. Phase 1 has been completed. Subjects who participated in Phase 1 have been transitioned to Phase 2, if they consented to do so. New subjects will only participate in Phase 2.

**Phase 1: MiniMed™ 780G insulin pump with Guardian 4 Sensor**

Phase 1 studied the MiniMed™ 780G insulin pump with Guardian 4 Sensor. See **Section 18.4.1** (Completed Study Design in **Appendix 4: Phase 1**) for the Study Design for Phase 1. This phase is now complete.

**Phase 2: MiniMed™ 780G BLE 2.0 insulin pump with DS5**

Phase 2 will study the MiniMed™ 780G BLE 2.0 insulin pump with the DS5. The combined run-in period and study period will be approximately 135 days long.

The period from Visit 1 (consent and screening) through Visit 8 should be completed within 45 days.

**Run-in Period (Visits 2-8):**

The run-in period begins at Visit 2 and ends once Visit 9 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, Humalog (insulin lispro injection), NovoLog/NovoRapid (insulin aspart solution for injection), or Admelog (insulin lispro injection).

During the run-in period of the study, subjects will be using the study pump in Manual Mode, with only the Sensor Augmented Pump (SAP) function activated (i.e., SmartGuard feature turned OFF). The "Suspend before Low" and "Suspend on Low" features may be used.

| Therapy at Screening | Pump Setting During Run-in Period |
|---|---|
| Continuous Subcutaneous Insulin Infusion (CSII) | Manual Mode |
| SAP (no closed loop) | Manual Mode |
| SAP (with closed loop [i.e., AID]) in non-Medtronic pump | Manual Mode |
| SAP (with closed loop) in Medtronic pump as Auto Mode | SmartGuard feature with Auto Correction OFF |

All subjects will be trained on diabetes management principles, such as the treatment of hyperglycemia and hypoglycemia. In addition, there will be training by investigational center staff regarding the need to have access to and how to use glucose and glucagon in case of hypoglycemia.

Companions/care partners will be instructed that they should be with the subject in the same residence or building complex overnight.

If the MiniMed Clinical/MiniMed Mobile app and the Carelink Clinical app are being used, companions/care partners 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 work, other activities. Instructions on the appropriate operation of the apps will be provided.

For study purposes, subjects will be instructed to perform self-monitoring of blood glucose (SMBG) if they are experiencing a severe hypoglycemic event, severe hyperglycemic event, hyperglycemic hyperosmolar syndrome (HHS), or diabetic ketoacidosis (DKA).

Blood ketones will be measured by all subjects using a ketone meter when:

- the subject is symptomatic for high blood glucose or
- the sensor glucose value is >300mg/dL, the BG is checked by fingerstick and, if BG is >300mg/dL, blood ketones should be checked

As a precaution, subjects 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 device issues (e.g., infusion set occlusion with high glucose).

Subjects will be instructed to insert study sensors only in the locations that are specified in the User Guide. Subjects should be reminded about appropriate study sensor placement at each office visit. Information about predominant location of study sensor insertions will be collected on an electronic case report form (eCRF) at the end of a subject's participation.

Subjects will be trained on all parts of the device system. Companions/care partners should be trained on how to respond to high or low glucose events. This should involve training conducted by investigational center staff. A training checklist for each subject should be completed by investigational center-based trainers. Companions/care partners should be available for relevant parts or, if desired, all of this training, either in person or virtually.

After completion of training on the study devices, subjects will be asked to attend additional visits in the days immediately following the start of system use, as needed. They may also take advantage of having continued access to the digital learning content, provided it is available at study start.

**Study Period (Visits 9-18):**
The study period begins at Visit 9 and ends at the conclusion of Visit 18.

Subjects will continue using the study pump and study sensor and will use the SmartGuard feature for approximately 90 days during the study period. Subjects should use the system with the

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

**Pump Settings:**
During the first 3 weeks (between Visits 9 and 14) of the study period, a 120 mg/dL Auto Basal Target should be used. It is recommended that Active Insulin Time is initially set to 4 hours and then titrated towards 2-3 hours at the investigator's discretion.

During the next 3 weeks (between Visits 14 and 16) of the study period, a 100 mg/dL Auto Basal Target setting should be used. Active Insulin time is recommended to be set to 2-3 hours or at investigator's discretion.

During the remaining weeks (any time after Visit 16) 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.

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

After completion of training on SmartGuard functions, subjects 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 digital learning content, provided it is available at study start.

**SMBG recommendations for 780G BLE 2.0 system:**
With the 780G BLE 2.0 system and the study sensor, calibration is not required. However, a calibration is optional, and it will automatically 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 SmartGuard. 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).

**Companions:**
Subjects will be required to have a companion (may be care partner) who resides (or will live) in the same building (or home) during the study at night. Companions should be able to check SMBG, give glucose and/or administer glucagon.

## 5.1 Duration

The study is anticipated to last approximately 36 months from first investigational center initiation to study period completion. Individual subject participation is expected to be approximately 135 days through the study period of each phase.

### 5.2 Rationale

Previous clinical investigations have confirmed the safety and clinical performance of the 780G insulin pump when used in a type 1 population in subjects 7 years of age or older. This investigation is intended to provide confirmation of the safety and clinical performance of the 780G system in a type 2 population in subjects 18-80 years of age.

## 6. Product Description

### 6.1 Intended Use

In this study, the MiniMed 780G system is intended for use by patients 18 years and older with type 2 diabetes who require at least 8 units and up to 250 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 | Device Status |
|---|---|---|
| MiniMed 780G Insulin Pump | MMT-1884* | Investigational |
| MiniMed 780G BLE 2.0 Insulin Pump | MMT-1884* | Investigational |
| Guardian 4 Sensor | MMT-7040 | Investigational |
| Guardian 4 Transmitter | MMT-7841 | Investigational |
| Disposable Sensor 5 (DS5) | MMT-5100 | Investigational |
| Medtronic Extended Reservoir | MMT-342 | Non-Investigational |
| Medtronic Extended Infusion Set | MMT-433 and MMT-443 | Non-Investigational |
| One-Press Serter | MMT-7512 | Non-Investigational |
| Charger | MMT-7715 | Non-Investigational |
| Tester | MMT-7736L | Non-Investigational |
| Medtronic CareLink Personal software | MMT-7333 | Non-Investigational |
| Medtronic CareLink system software | MMT-7350 | Non-Investigational |
| Roche Accu-Chek Guide Link Glucose Meter | 08116083022, 09651926001M, 09651942001M | Non-Investigational |
| MiniMed Clinical App | MMT-6103 Android; MMT-6104 IOS | Non-Investigational |
| CareLink Clinical App | MMT-6113 Android; MMT-6114 IOS | Non-Investigational |
| MiniMed Mobile App | MMT-6101 Android; MMT-6102 IOS | Non-Investigational |
| Blue Adapter | ACC-1003911 | Non-Investigational |
| Ketone Meter | -- | Non-Investigational |

*Note: Although the model numbers for the insulin pumps (780G and 780G BLE 2.0) are the same, each has a unique model number extension.

## 6.3 Investigational Product

### 6.3.1 MiniMed 780G Insulin Pump

The MiniMed 780G Insulin Pump houses electronics, a pumping mechanism, a user interface, and a medication reservoir within the same physical device. The pump communicates via Bluetooth® Low Energy wireless communication protocol with the compatible devices in the MiniMed 780G System. In this study, the MiniMed 780G Pump System components will interact as follows (MiniMed 780G System and components presented in **Figure 2** [MiniMed 780G BLE 2.0 insulin pump with DS5]) and **Figure 3** [MiniMed 780G insulin pump with Guardian 4 CGM]):

- **Phase 1:** The MiniMed 780G insulin pump receives the SG values and sensor integrity check from the Guardian 4 Transmitter, which is connected to the Guardian 4 sensor.
- **Phase 2:** The MiniMed 780G BLE 2.0 insulin pump receives the SG values and sensor integrity check from the DS5.
- 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/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/MiniMed Mobile app.

**Figure 2. 780G BLE 2.0 System with DS5 CGM**

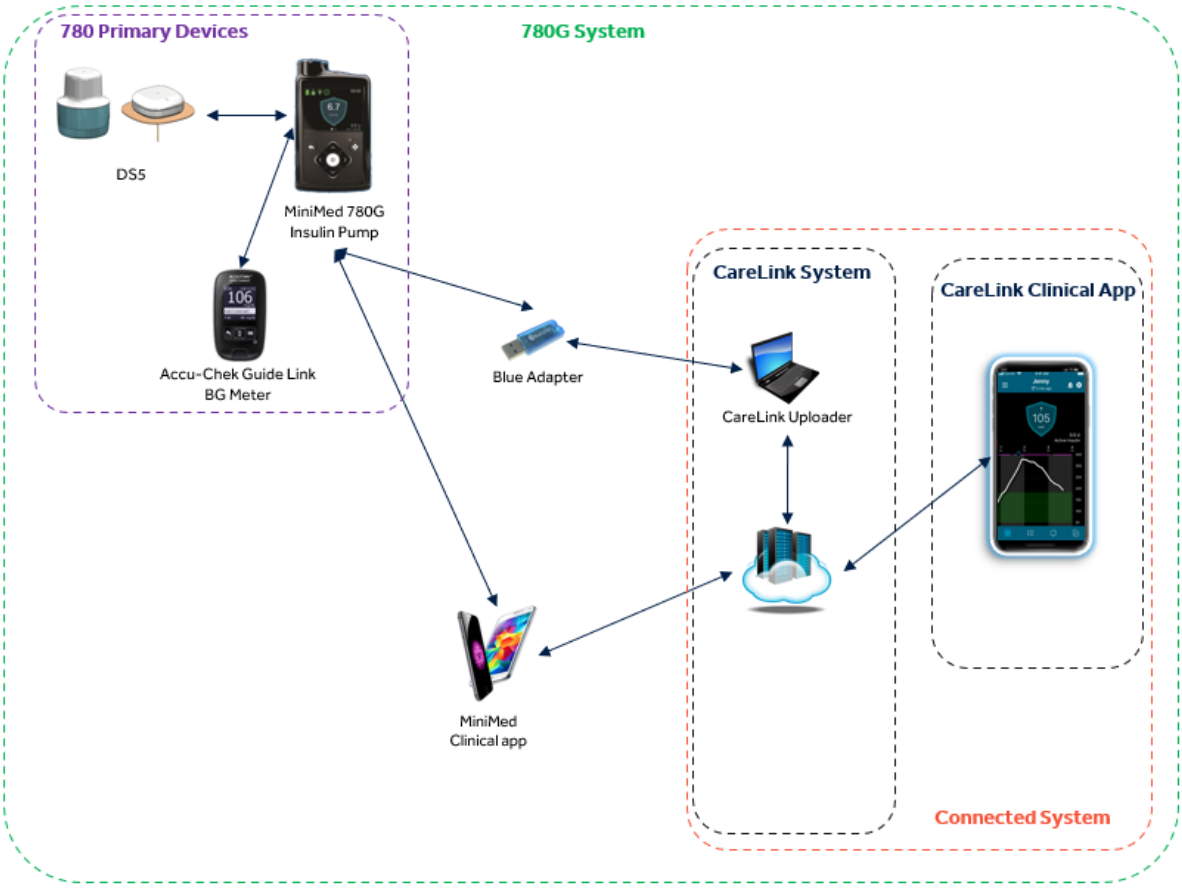
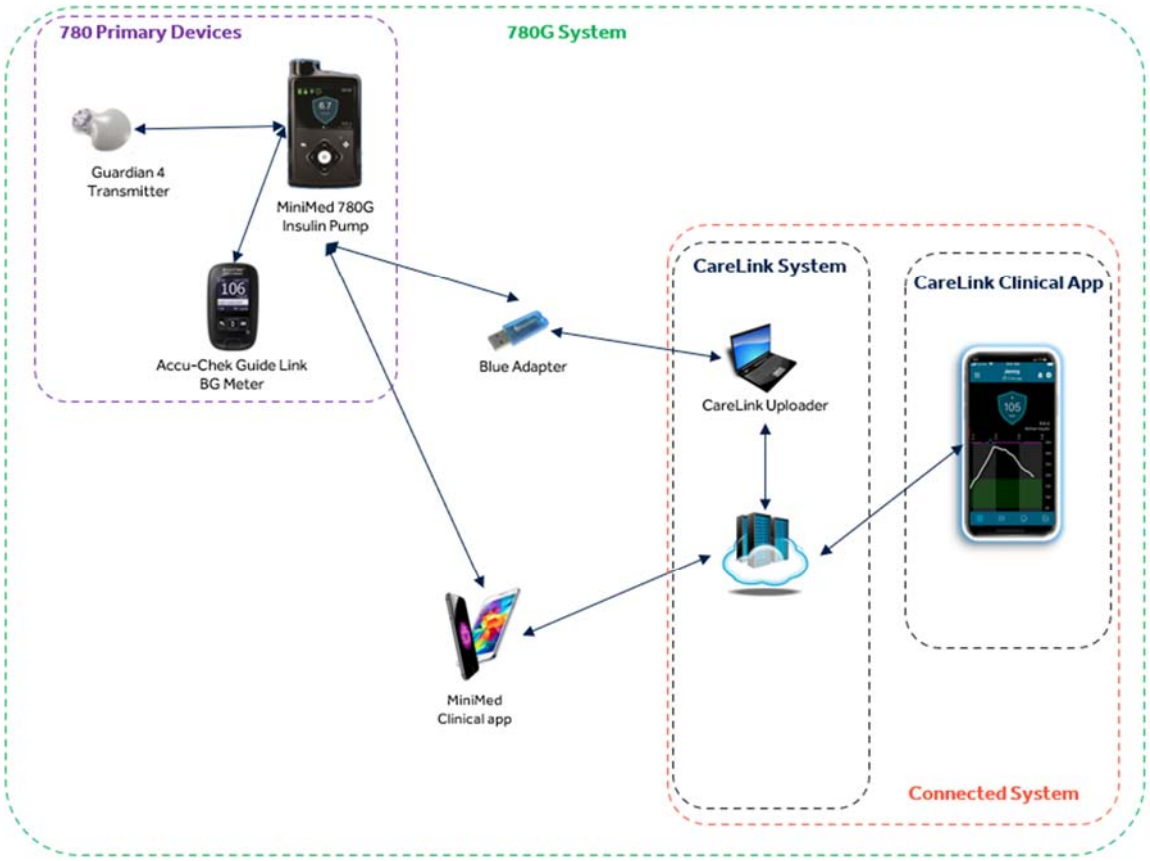


**Figure 3. 780G System with Guardian 4 CGM**




### 6.3.2 Guardian 4 Sensor

The Guardian 4 sensor, referred to as the study 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.

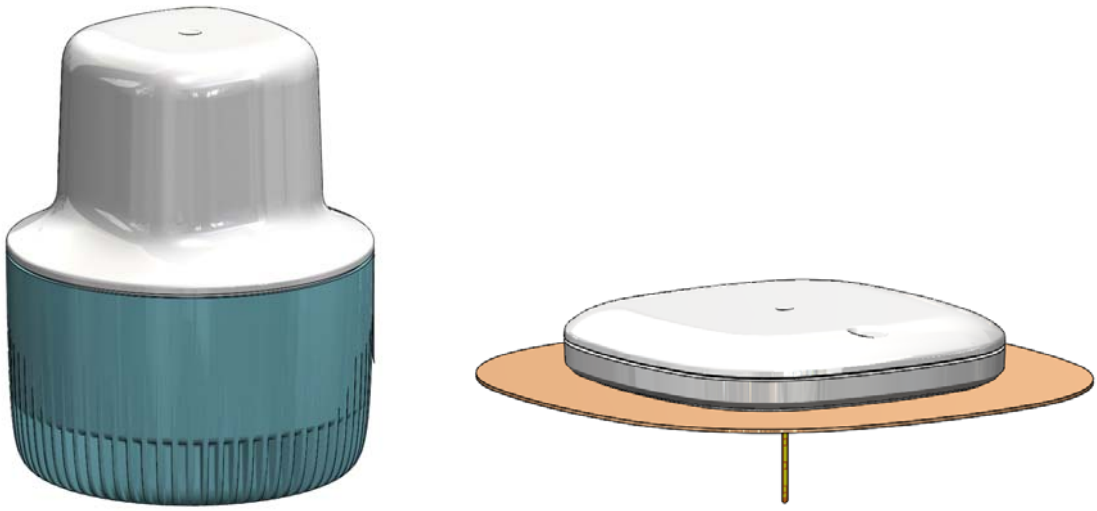
### 6.3.3 Guardian 4 Transmitter

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 sensor integrity (SI) data from the sensor to compatible insulin pumps via a Bluetooth Low Energy wireless communication protocol.

### 6.3.4 Disposable Sensor (DS5)

The Disposable Sensor, referred to as study sensor in this CIP, is a disposable integrated sensor-transmitter platform. The sensor is packaged into a single-use insertion device, called the inserter, resulting in an all-in-one device out of the box. The inserter is designed to simplify the insertion process. The sensor flex is inserted subcutaneously with an introducer needle, which is retracted by the inserter upon removal. The sensor wirelessly sends the collected sensor data to the MiniMed 780G BLE 2.0 insulin pump or other compatible mobile device.

**Figure 4. DS5**



## 6.4 Non-Investigational Product(s)

### 6.4.1 Medtronic Extended Infusion Set

Infusion sets are single-use by patients with diabetes mellitus requiring subcutaneously 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 Extended 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

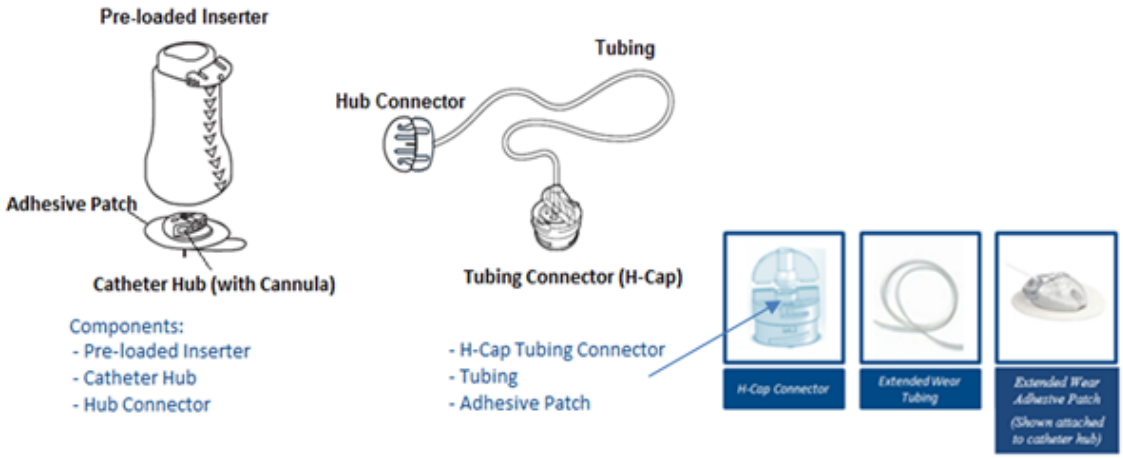
The cannula, connected to the catheter hub, is introduced into subcutaneous tissue (i.e., infusion site). The tubing connects the catheter hub and the tubing connector to provide the fluid from the medication reservoir housed within the insulin pump.

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 5** illustrates 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).

In this study, subjects may use the Medtronic Extended infusion set or other approved Medtronic infusion sets (see **Section 6.6**).

**Figure 5. Medtronic Extended Infusion Set**




### 6.4.2 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. In this study, subjects may use the Medtronic Extended Reservoir or other approved Medtronic reservoirs (see **Section 6.6**).

### 6.4.3 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 study 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.

### 6.4.4 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.

### 6.4.5 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.

### 6.4.6 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 uses 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.

### 6.4.7 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 uses 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.

### 6.4.8 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.

### 6.4.9 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/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/MiniMed Mobile app screen, for remote monitoring by a care partner (e.g., companion). 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.

### 6.4.10 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/MiniMed Mobile app are not possible.

### 6.4.11 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.

## 6.5 Smartphone

Sponsor may provide a smartphone and/or tablet, upon request.

## 6.6 Consumable Devices

Glucose meter accessories, Medtronic infusion sets, Medtronic reservoirs, and other consumable materials will be provided to subjects for use in the study.

## 6.7 Insulin

Subjects will use their own rapid-acting analogue insulin (Novolog, Humalog, or Admelog) for this study.

## 6.8 Anticipated Product Changes

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

## 6.9 Product Accountability

Good Clinical Practice (GCP) 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 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 2**.

**Table 2. Product Accountability Requirements**

| Device | Record on Site Received eCRF | Record Disbursement, Returned or Not Returned from Subject on Subject Device Identification eCRF | Subject Return Device to Investigational Center | Record Returned or Not Returned to Sponsor on Site Returned eCRF | Investigational Center Return Device to Sponsor at Conclusion of Study |
|---|---|---|---|---|---|
| MiniMed 780G Insulin Pump (MMT-1884) | Yes | Yes | Yes | Yes | Yes |
| MiniMed 780G BLE 2.0 Insulin Pump (MMT-1884) | Yes | Yes | Yes | Yes | Yes |
| Guardian 4 Sensor (MMT-7040) | Yes | Yes | Yes (Complaint and unused) No* (Non- | Yes | Yes (Unused) No* (Used) |

| Device | Record on Site Received eCRF | Record Disbursement, Returned or Not Returned from Subject on Subject Device Identification eCRF | Subject Return Device to Investigational Center | Record Returned or Not Returned to Sponsor on Site Returned eCRF | Investigational Center Return Device to Sponsor at Conclusion of Study |
|---|---|---|---|---|---|
| | | | complain used) | | |
| Guardian 4 Transmitter (MMT-7841) | Yes | Yes | Yes | Yes | Yes |
| DS5 (MMT-5100) | Yes | Yes | Yes (Complaint and unused) No* (Non-complaint used) | Yes | Yes (Complaint and unused) No* (Non-complaint used) |
| Roche Accu-Chek Guide Link Study Meter (08116083022, 09651926001M, 09651942001M) | Yes | Yes | Yes | Yes | No* |
| Ketone Meter | Yes | Yes | Yes | Yes | No* |
| Smartphone, as approved for distribution | Yes | Yes | Yes | Yes | Yes |
| Tablet, if distributed | Yes | N/A | N/A | Yes | Yes |

*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.

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.

### 6.9.1 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 2.**

### 6.9.2 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.

### 6.9.3 Dispensing of Study Devices

Each time a study device 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

### 6.9.4 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 2** 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 2**. 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.

# 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 principal 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:

- IRB approval (and voting list, as required by local law) of the current version of the Clinical Investigation Plan (CIP) and Informed Consent Form (ICF), and report of prior investigations
- 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 575 subjects, with at least 300 subjects entering the study period of Phase 2, with insulin-requiring type 2 diabetes age 18-80 will be enrolled at up to 40 investigational centers across the United States.

To widen the distribution of the type 2 diabetes population, investigational centers are encouraged to enroll a study population that represents a wide variety of races, ethnicities, BMI, TDD of insulin, and background diabetes medications.

## 8.2 Subject Enrollment

Subjects will be considered enrolled in the study upon signing the ICF.

A subject will be assigned a unique study subject ID via the eCRF, which is a 9-digit code (341XXXXXX). The first three digits refer to the CIP number (341), the next three digits refer to the investigational center number, and the last 3 digits refer to the subject number assigned during Visit 1 (e.g., 341002001 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. Is age 18 – 80 years at time of screening.
2. Has a clinical diagnosis of type 2 diabetes for 2 years or more as determined via medical record or source documentation by an individual qualified to make a medical diagnosis.
3. Is on MDI regimen (basal/bolus regimen with long-acting insulin and rapid-acting analogs), defined as greater than or equal to 2 injections per day for at least 3 months prior signing the informed consent, or CSII pump therapy with or without CGM. The investigator will use their discretion to verify that insulin requirements have been stable for the last 3 months prior to screening.
4. Is able to comply with technology, according to Investigator's judgment
5. Does not require a legally authorized representative to consent on their behalf due to mental or intellectual disability.
6. Is willing to perform fingerstick blood glucose measurements as needed.
7. Is willing to wear the system continuously throughout the study.
8. Has a Glycosylated hemoglobin (HbA1c) of 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.
9. 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.

10. 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.
11. Is willing to take one of the following insulins and can financially support the use of insulin preparations as required by the study:
    a) Humalog (insulin lispro injection)
    b) NovoLog/NovoRapid (insulin aspart injection)
    c) Admelog (insulin lispro injection)

## 8.4 Exclusion Criteria

1. 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
2. Has been hospitalized or has visited the ER in the 6 months prior to screening resulting in a primary diagnosis of uncontrolled diabetes.
3. Has had diabetic ketoacidosis (DKA) or hyperglycemic hyperosmolar syndrome (HHS) in the last 6 months prior to screening visit.
4. Will not tolerate tape adhesive in the area of sensor placement as assessed by a qualified individual.
5. Has any unresolved adverse skin condition in the area of sensor placement (e.g., psoriasis, dermatitis herpetiformis, rash, Staphylococcus infection) at time of screening.
6. Has (Total Daily Dose) of less than 8 units or greater than 250 units at time of screening.
7. Has positive GAD (Glutamic Acid Decarboxylase) Antibody test
8. Is female of child-bearing potential and result of pregnancy test is positive at screening
9. Is sexually active female of child-bearing potential and is not using a form of contraception deemed reliable by the investigator.
10. Is female and plans to become pregnant during the course of the study.
11. Is being treated for hyperthyroidism at time of screening.
12. Has diagnosis of adrenal insufficiency at time of screening.
13. 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.
    **Note:** Intra-articular injections to treat pain (e.g., joint pain, bursitis, etc.) are permitted
14. Is using hydroxyurea at time of screening or plans to use it during the study.
15. 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 prior to screening. (**Note:** Did not apply to subjects who transitioned from Phase 1 to Phase 2).
16. Is currently abusing illicit drugs.
17. Is currently abusing marijuana.
18. Is currently abusing prescription drugs.
19. Is currently abusing alcohol.
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 greater than CKD2 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 prior to 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. Subject may be enrolled if clearance from a board-certified cardiologist is provided prior to or at Screening.
32. Is a member of the research staff involved with the study.
33. Has used a MiniMed 780G pump prior to screening (**Note**: In Phase 2, this applies to new subjects only).

# 9. Study Procedures

## 9.1 Schedule of Events

Subjects may participate in 2 phases.

**Phase 1 (Completed)**: Subjects participated in a minimum of 18 planned study visits, as presented in **Section 18.4.3**, for approximately 135 days of device wear. Subjects were allowed to enter a continued access period, following the end of the study period. Phase 1 has been completed. For detailed information, see **Section 18.4 Appendix 4: Phase 1**.

**Phase 2:** Subjects will participate in a minimum of 18 planned study visits, as presented below in **Figure 6**, for approximately 135 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.

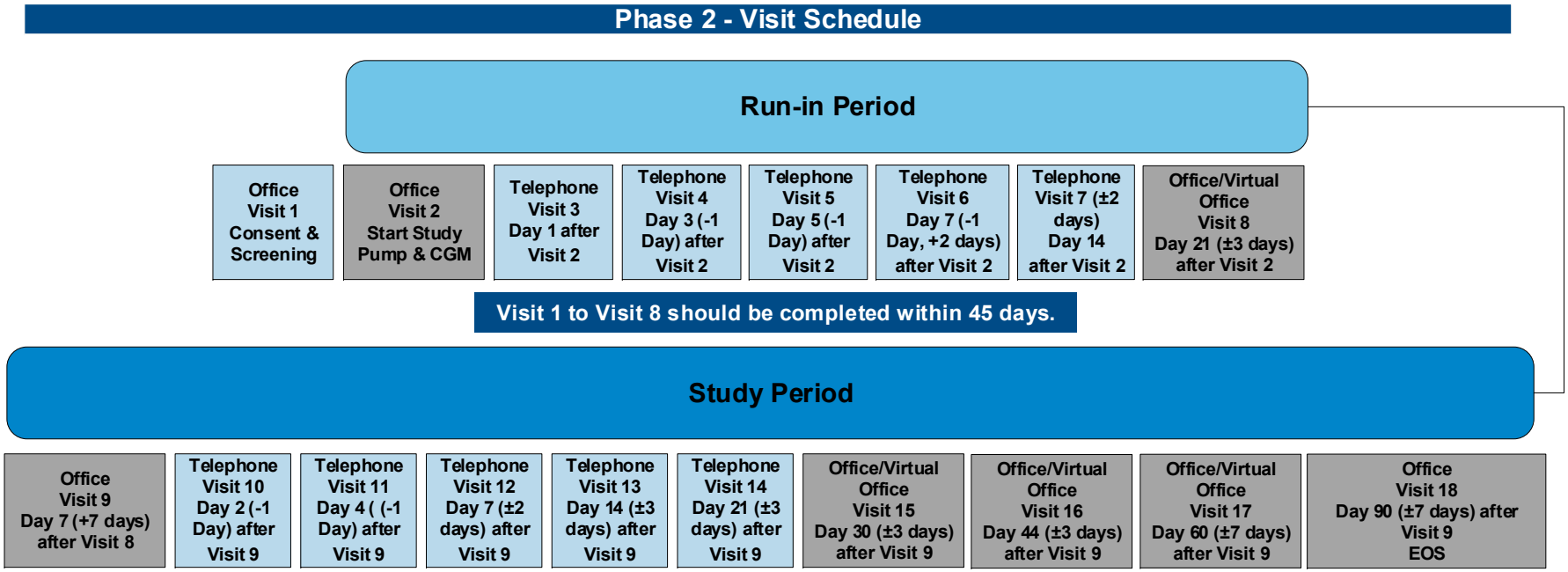
If subject exits the study early (i.e., before their last scheduled visit), HbA1c requirements that apply to the final visit will be completed for subjects who have completed Visit 9. Refer to CIP341 Questionnaire Guide for collection of early exit survey/questionnaire requirements.

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

**Subjects who transitioned from Phase 1 to Phase 2:**
Phase 1 subjects were given the opportunity to transition into Phase 2 upon completion of the Phase 1 study period or at a subsequent continued access period visit. Transitioning subjects were expected to complete all required Visit 1 – Phase 2 activities prior to entering Visit 9 – Phase did not need to complete Visit 2 through Visit 8 of Phase 2.

Refer to **Section 9.1.1**, **Table 3** for the Visit Details.

**Figure 6. Phase 2 Visit Schedule**




**Note:** Phase 1 subjects were given the opportunity to transition into Phase 2 upon completion of Phase 1 – Study Period or at a subsequent continued access period visit. Phase 1 is now complete and the Phase 1 visit schedule is presented in **Section 18.4.2** for reference.

### 9.1.1 Study Visit Schedule & Scheduled Follow-Up Visit Windows

**Visit 1 to Visit 8 should be completed within 45 days.**

- Visit 1 (Office): Consent and screening
  - Collect labs

**Run-In Period:**

- Visit 2 (Office): Start Run-In
  - Eligibility has been confirmed
  - Start study pump and CGM in Manual Mode
  - Register and upload study pump in CareLink Personal and CareLink system
  - Ask subjects about adverse events and device performance

- Visit 3 (Phone): Day 1 after Visit 2
  - Ask subjects if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 4 (Phone): Day 3 (-1 day) after Visit 2
  - Ask subjects if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 5 (Phone): Day 5 (-1 day) after Visit 2
  - Ask subjects if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 6 (Phone): Day 7 (-1, +2 days) after Visit 2
  - Ask subjects if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 7 (Phone): Day 14 (±2 days) after Visit 2
  - Ask subjects if they required assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 8 (Office/Virtual Office): Day 21 (±3 days) after Visit 2
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

**Study Period:**

- Visit 9 (Office): Start Study Period, Day 7 (+7) after Visit 8

  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Start subjects on SmartGuard
  - Start auto basal target at 120 mg/dL

- Visit 10 (Phone): Day 2 (-1 day) after Visit 9
  - Adjust pump settings as needed
  - Ask subjects if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 11 (Phone): Day 4 (-1 day) after Visit 9
  - Adjust pump settings as needed
  - Ask subjects if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 12 (Phone): Day 7 (±2 days) after Visit 9
  - Adjust pump settings as needed
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 13 (Phone): Day 14 (±3 days) after Visit 9
  - Adjust pump settings as needed
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 14 (Phone): Day 21 (±3 days) after Visit 9
  - Adjust pump settings as needed
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Change auto basal target at 100 mg/dL setpoint

- Visit 15 (Office/Virtual Office): Day 30 (±3 days) after Visit 9
  - Adjust pump settings as needed
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 16 (Office/Virtual Office): Day 44 (±3 days) after Visit 9
  - Adjust Auto Basal target with Active Insulin Time at investigator's discretion
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 17 (Office/Virtual Office): Day 60 (±7 days) after Visit 9
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 18 (Office): Day 90 (±7 days) after Visit 9
  - Collect HbA1C
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Return study devices
  - End of Study (EOS)

**Table 3. Phase 2 Study Visit Details**

| | | Run-In Period | | | | | Study Period | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Visit 1 (Office) | Visit 2 (Office) | Visit 3, 4 & 5 (Phone) | Visit 6 (Phone) | Visit 7 (Phone) | Visit 8 (Office/Virtual Office) | Visit 9 (Office) | Visit 10 & 11 (Phone) | Visit 12, 13 & 14 (Phone) | Visit 15 & 16 (Office/ Virtual Office) | Visit 17 (Office/Virtual Office) | Visit 18* (Office) |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 End of Study** |
| Collect consent forms, e.g., ICF, 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<br>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. All collected blood specimens will be sent to and tested by a NGSP certified Central Laboratory. Testing must follow NGSP standards.<br>Note: If the visit must be conducted via Virtual Office, the blood tests may be collected via mobile phlebotomy service. | X | | | | | | | | | | | X |
| Collect specimens for required local lab testing: Hematocrit, Creatinine, TSH, GAD, c-peptide (Note: c-peptide is not part of inclusion/exclusion criteria) – 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 (including the type of insulin being used). The only insulins permitted for use in the study are Humalog, Novolog/NovoRapid, and Admelog. | | 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) |

| | | Run-In Period | | | | | Study Period | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/Virtual Office)** | **Visit 18* (Office)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 End of Study** |
| Confirm subject eligibility results, including labs, prior to moving forward with any study procedures | | X | | | | | | | | | | |
| Assist with Questionnaires – Refer to CIP341 Questionnaire Guide for administration details. | | X | | | | | 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 |
| 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 |
| Train subjects on the use of the Accu-Chek Guide Link study meter and ketone meter, refer to user guides | | X | | | | | | | | | | |
| Train subjects on the use of the 780G BLE 2.0 insulin pump with DS5 | | X | | | | | | | | | | |
| Start study subjects on the 780G BLE 2.0 insulin pump system (Manual Mode) | | X | | | | | | | | | | |
| Provide study subjects the Medtronic infusion sets, reservoirs, sensors and transmitter | | X | | | | As needed | As needed | | | As needed | As needed | As needed |
| Train subjects on the Medtronic infusion sets, reservoirs, sensors and transmitter | | X | | | | | | | | | | |
| Start study subjects on CGM (transmitter and sensor) and accessories | | X | | | | | | | | | | |
| Instruct subjects 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 | If applicable |
| Train study subjects on the 780G BLE 2.0 SmartGuard features. | | | | | | | X | | | | | |
| Instruct subjects on the SmartGuard feature of the pump as well as specific considerations regarding SmartGuard:<br>• Ensure that the Auto Correction feature is turned ON and remains ON throughout the course of the study.<br><br>Instruct subjects to switch from pump therapy to manual injections until issue is resolved if: | | | | | | | X | | | | | |

| | | Run-In Period | | | | | Study Period | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/Virtual Office)** | **Visit 18* (Office)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 End of Study** |
| • Hospital admission is needed for any reason<br>• Glucose is persistently elevated (i.e., above 300 mg/dL) and not responding to correction boluses and/or infusion set change(s).<br>• 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 | | X | As needed | As needed | As needed | As needed | X | As needed | As needed | As needed | 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 | | | | | | | | | | |
| Train subjects on the use of CareLink Personal–provide relevant set of written instructions | | X | | | | | | | | | | |
| Set up 780G BLE 2.0 system apps, if applicable:<br>• MiniMed Clinical/MiniMed Mobile app<br>• CareLink Clinical app | | X | | | | | | | | | | |
| If applicable:<br>Train subjects and companions/care partners on the use of the 780G BLE 2.0 system apps: MiniMed Clinical/MiniMed Mobile app and CareLink Clinical app | | X (if applicable) | | X (if applicable) | | X (if needed) | | | | | | |
| If applicable:<br>For subjects who are currently using SGLT inhibitors, the investigational center will provide training as well as a wallet card-formatted STICH protocol. | | 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) |
| Start Auto Basal Target = 120 mg/dL with Active Insulin Time = 4 hours-titrated towards 2-3 hours at investigator's discretion at Visit 9 | | | | | | | X | | | | | |

| | | Run-In Period | | | | | Study Period | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/Virtual Office)** | **Visit 18* (Office)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 End of Study** |
| Start Auto Basal Target = 100 mg/dL with Active Insulin Time = 2-3 hours or at investigator's discretion at Visit 14 | | | | | | | | | X (Visit 14) | | | |
| Dispense study materials (e.g., smartphone [upon request and approval], reference guides, subject training materials, etc.) | | X | | | | | X | X | X | | | |
| Dispense other study supplies as needed (e.g., alcohol swabs, adhesive remover, etc.) | | X | | | | As needed | 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 | 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 |
| Review CareLink system reports | | | X | | | X | X | X | | X | X | If applicable |
| 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 | |
| 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 | If applicable |
| Collect study devices at study end (see device disposition **Table 2** for details).<br>Note: If the visit must be conducted via Virtual Office, the blood tests may be collected via mobile phlebotomy service. Subjects should send devices back to the investigational center. | | | | | | | | | | | | X |
| Ask if subjects 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.<br>• 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<br>• 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 |

| | | Run-In Period | | | | | Study Period | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/Virtual Office)** | **Visit 18* (Office)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 End of Study** |
| Ask subjects about device performance issues and if they called the Medtronic 24 -Hour Technical Support (TS) line to report them.<br>Instruct/Remind subjects to contact the Medtronic 24-Hour TS in the event they experience problems with their study devices. | | X | X | X | X | X | X | X | X | X | X | X |
| Ask subjects if they require assistance, e.g., additional training | | | X | X | X | X | | X | | | | |
| Ask subjects about the use of SGLT inhibitors during the Continued Access Period | | | | | | | | | | | | |
| Remind subjects that the use and wear of study devices throughout the study is a requirement | | X | X | X | X | X | X | X | X | X | X | If applicable |
| Instruct/Remind subjects regarding the content of the Home Reference Guide | | X | | | | | | | | | | |
| Instruct subjects on carbohydrate (CHO) counting as needed (Investigator discretion) | | X | X | X | X | X | X | X | X | X | X | If applicable |
| Instruct subjects on diabetes self-management principles including response to glycemic events, e.g., use of oral glucose/glucagon in case of severe hypoglycemia or checking for ketones in case of severe hyperglycemia<br>Note: Companions/care partners should be trained on how to respond to high or low glucose events. | | X | | | | | | | | | | |
| Instruct subjects and companions/care partners that blood ketone testing is required every time BG is greater than 300 mg/dL, as measured by the Accu-Chek Guide Link study meter. | | X | X | X | X | X | X | X | X | X | X | If applicable |
| Instruct subjects to consider avoiding the use of products containing acetaminophen.<br>If medications containing acetaminophen are taken:<br>• Wait until use of the medication is stopped before using SG to make treatment decisions<br>• Use additional BG meter readings to verify glucose levels | | X | X | X | X | X | X | X | X | X | X | If applicable |

| | | Run-In Period | | | | | Study Period | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/Virtual Office)** | **Visit 18* (Office)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 End of Study** |
| • While the SmartGuard feature is active, instruct subjects to use the temp target feature (when used, Auto Correction is not available)<br>• Instruct subjects that in case of prolonged use of acetaminophen, the temp target feature can be used repeatedly and in succession | | | | | | | | | | | | |
| Remind subject to bring in both Accu-Chek Guide Link study meter and ketone meter at each required office visit. | | X | | | X | X | | | X | X | X | If applicable |
| Remind subject to keep their devices charged, as applicable | | X | X | | | X | X | X | | X | X | If applicable |
| Instruct subjects regarding the use of the Accu-Chek Guide Link study meter to make treatment decisions:<br>• When a BG required alert is received:<br>○ Clear the alert and enter a BG meter reading before using the SG to make treatment decisions<br>• When symptoms are present:<br>○ If SG readings are not aligned with symptoms (e.g., if a study subject is feeling low while the SG reading is not low), use the meter to confirm BG.<br>○ If SG readings continue to be different from symptoms, call the study doctor | | X | X | | | X | X | X | | X | X | If applicable |
| Instruct subjects 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 that they should not assume that SmartGuard is able to prevent all hypoglycemia or all hyperglycemia including diabetic ketoacidosis and HHS | | X | | | | | X | | | X | X | If applicable |

| | | Run-In Period | | | | | Study Period | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/Virtual Office)** | **Visit 18* (Office)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 End of Study** |
| Instruct study subjects that regular weekly uploads of the study pump is required. With Bluetooth connection and the MiniMed Clinical/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. | | X | X | X | X | X | X | X | X | X | X | If applicable |
| Instruct subjects to give meal bolus of insulin 15-20 minutes before meals during the run-in period and study period | | X | X | X | X | X | | | | | | |

*Note: When subjects exit the study early during the study period, all requirements that are listed for Visit 18 apply.

**Note: Office visits should be completed unless there are circumstances that may put patients at risk or where in person visits may not be allowed.

## 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 will be obtained in accordance with the Code of Federal Regulations (CFR) Title 21, Part 50. Prior to entry into the study, the California Experimental Subject's Bill of Rights (if applicable), the Institutional Review Board (IRB) and Medtronic approved ICF form and an Authorization Form required by the Health Insurance Portability and Accountability Act (HIPAA) will be presented to each subject to review and sign as applicable. The subject will be given ample time and offered the opportunity to review these documents away from the investigational center.

The following will be provided to or explained to the subject 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 questions during the informed consent process. The language used shall be as non-technical as possible and must be understandable to the subject.

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

Subjects will complete California Experimental Subject's Bill of Rights (if applicable), the HIPAA Form, and the ICF. The consenting process must be documented in the subject's source documents. The subject 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 a in a timely manner.

Medtronic will revise the written ICF 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 IRB. After approval by the IRB, a copy of this information must be provided to the participating subjects, and the informed consent process as described above needs to be repeated.

If the ICF is amended during the course of the study, the IRB will determine:

- Whether or not active subjects 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 will be informed that qualified personnel from the investigational center, the sponsor (Medtronic), regulatory authorities such as the FDA and/or the 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 violations to their IRB and sponsor:

- Failure to obtain informed consent from subject.
- Failure to obtain informed consent prior to performing one or more study procedures.
- Failure to maintain ICFs forms on file for all subjects who have provided informed consent.
- Use of an ICF form that has not received approval from the IRB.
- Use of an incorrect version of the ICF 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**.

### 9.4.3 Calibration of CGM Risk

When an erroneous blood glucose value is entered, which then calibrates the CGM, it can result in an inaccurate SG value. Subjects will be trained accordingly.

### 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**.

### 9.4.8 HbA1c Risk

A Central laboratory will be used for HbA1c testing.

### 9.4.9 Risks Associated with Rapid Weight Loss

Subjects who undergo a weight loss regimen that includes GLP-1 and other drugs may be subject to glycemic variability. Investigators should use their discretion to make sure that any such regimen is stable and does not cause additional risk to study subjects.

### 9.4.10 Transition of Subjects on MDI Therapy To/From Pump Therapy

To assist subjects who enter the study on MDI therapy, investigators and their staff will be instructed on best practices regarding the safe transition from MDI therapy to pump use at the start of the study and a safe transition back to MDI therapy at the end of the study.

For subjects transitioning from MDI to Pump:

- Consider reducing MDI total daily dose by 25% to calculate pump total daily dose before calculating pump settings
- Consider instructing subjects not to administer their long-acting insulin dose the night before/morning of the scheduled pump start.
    - If pump therapy is initiated within 24-36 hours of the last long-acting insulin injection (depending on the duration of action of the brand administered), consider setting a temporary basal rate of 0% to run until that time has passed

For subjects transitioning back to MDI therapy after study participation ends:

- Consider recalculating injection doses based on pump settings, or returning to that subject's previous MDI dose schedule and adjust as needed

### 9.4.11 Risk Associated with Non-Insulin Anti-Diabetic Medications

If, during the study period with AHCL therapy, the time below 70 mg/dL exceeds 4% for individual study subjects, investigator should use their clinical discretion and also consider changing pump settings. In addition to changing pump settings, investigators might also consider dose reductions or stopping the use of one or both of these two classes of medications (sulfonylureas &/or meglitinides) for individual subjects.

### 9.4.12 Risk Associated with SGLT Therapy

For subjects who are currently using SGLT inhibitors, the investigational center will provide training as well as a wallet card-formatted STICH protocol. The STICH protocol warns patients who are taking SGLT inhibitors about the risks associated with this therapy relative to the occurrence of ketosis and DKA.

## 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:

- the subject is symptomatic for high blood glucose or
- the sensor glucose is >300 mg/dL, the BG should be checked by fingerstick, if BG is >300 mg/dL, 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 9 and exit early, labs will be collected. In the continued access period, HbA1c were collected every 90 days.

## 9.6 Recording Data

Data, except questionnaires, 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/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/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 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.

If there is a documented safety reason that would not permit the use of CIP defined Auto Basal target setting and Active Insulin Time settings, then use of the alternative settings will not be considered a deviation.

### 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 5** for reporting timelines for emergency deviations.

CIP deviations should be reported as follows:

a) To the 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 (21 CFR 812.140 Records).

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, i.e., there is no documentation of consenting
- Informed consent 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 IRB
- Failure to inform IRB and sponsor of reportable AEs (see **Section 11**)
- Investigational study device dispensed without obtaining informed consent

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 the IRB as well as Medtronic within five (5) working days.

Reporting of all other study deviations should comply with:

- 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 5**, for specific deviation reporting requirements and timeframes for reporting to Medtronic, 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 uses insulin that is not allowed to be used in the study. The only permitted insulins are Humalog, Novolog/NovoRapid and Admelog.
- 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 repeatedly 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 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 run-in period, 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. (Note: Intra-articular injections to treat pain (e.g., joint pain, bursitis, etc.) are permitted.)
    - Exception: During the continued access period in Phase 1 of the study, subjects will be allowed to receive orally administered steroid treatments for a maximum of 2 weeks. Intra-articular injections to treat pain (e.g., joint pain, bursitis, etc.) continue to be permitted. Duration of use as well as type of steroid used must be documented on the Concomitant Medications CRF.
- 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 MiniMed 780G system SmartGuard feature.
- During the study, the subject experiences one episode of DKA or HHS, if it is related to the use of MiniMed 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 (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 investigational center for required follow-up visit(s) and cannot be reached, the investigational center staff 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 investigational center, 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 center staff to collect all study devices and supplies back from subject, if applicable.

## 9.9 Study Stopping Rules

The study may be stopped if the Data Monitoring Committee (DMC) determines that there are significant safety issues, including the occurrence of certain types of individual adverse events (i.e. UADE, device related DKA, device related HHS and device related Severe Hypoglycemia) that have undergone expedited adjudication by the Clinical Events Committee (CEC). See CEC **Section 12.1** and DMC **Section 12.2** for more details regarding the expedited review responsibilities of both committees.

# 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 4**. 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.

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 4. Risks, Prevention and Mitigation**

| Risks with Infusion Sets | Prevention and Mitigation |
|---|---|
| Risks with infusion sets may include:<br><br>• Localized infection<br>• Skin irritation/redness<br>• Bruising<br>• Discomfort/pain<br>• Bleeding<br>• Irritation<br>• Rash<br>• Hyperglycemia secondary to infusion set occlusion or infusion site failure including DKA or HHS<br>• Hyperglycemia secondary to site falling off including DKA or HHS<br>• Anxiety associated with insertion | Prevention and mitigation include:<br><br>• Follow the provided user guides for insertions and care of infusion sets.<br>• If an infusion site becomes irritated or inflamed, the infusion set will be removed and another set placed in a new location.<br>• 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.<br>• Follow the provided user guides for insulin pump management.<br>• 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 administration of too much or too little insulin which can lead to the following clinical consequences:<br><br>• Hypoglycemia<br>• Hyperglycemia<br>• Diabetic ketoacidosis or HHS<br>• Severe hypoglycemia with or without associated seizure, coma or death<br>• Kinked cannula leading to hyperglycemia<br>• Infusion set disconnection from pump leading to hyperglycemia<br>• Subject removes the reservoir from the pump but forgets to disconnect the infusion set from the body which results in hypoglycemia or severe hypoglycemia<br>• Dislodged cannula leading to hyperglycemia<br>• A pump error may lead to under delivery or over-delivery of insulin<br>• Battery failure – no insulin delivered<br>• Insulin deterioration leading to hyperglycemia<br>• Incomplete priming; fails to prime tubing and/or cannula, leading to hyperglycemia | Prevention and mitigation include:<br><br>• Follow the provided user guides & instructions for insulin and insulin pump management which includes information on infusion set change.<br>• Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems.<br>• 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.<br>• Instruct to check their meter glucose if there are any concerns that the SG value is not accurate.<br>• Instruct to have glucose and glucagon on hand for hypoglycemia.<br>• Instruct to change infusion set if suspected catheter occlusion or administer insulin with syringe for persistent hyperglycemia especially if ketones develop. |

| | |
|---|---|
| • Remove a reservoir, without suspending and reconnecting after a while resulting in a hypoglycemia<br>• Patient not filling pump reservoir when needed leading to hyperglycemia<br>• Magnetic resonance imaging resulting in pump transmitter malfunction<br>• Inaccurate insulin delivery due to sudden altitude changes.<br>• Hypoglycemia or hyperglycemia from manual bolus<br>• Hypoglycemia or hyperglycemia from the use of the SmartGuard feature where SG values may be used to calculate insulin bolus amounts<br>• Hypoglycemia or hyperglycemia from computer hacking | |
| Risks with hyperglycemia may include:<br><br>• Diabetic ketoacidosis or HHS<br>• Symptomatic ketosis<br>• Cardiovascular event<br>• Dehydration<br>• Potassium and sodium imbalance<br>• Shock<br>• Altered mental status<br>• Coma<br>• Acidosis | Prevention and mitigation include:<br><br>• Follow the provided user guides for insulin pump management.<br>• Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems.<br>• 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.<br>• Instruct to check their meter glucose if there are any concerns that the SG value is not accurate.<br>• Alternative method of managing glucose levels will be available (insulin and syringe for example). |
| Risks with hypoglycemia may include:<br><br>• Seizure<br>• Coma<br>• Altered mental status<br>• Loss of consciousness<br>• Cardiovascular event<br>• Death<br>• Risk of rebound hyperglycemia with ketosis | Prevention and mitigation include:<br><br>• Follow the provided user guides for insulin pump management.<br>• Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems.<br>• 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.<br>• Instruct to check their meter glucose if there are any concerns that the SG value is not accurate).<br>• Instruct to have glucose and glucagon on hand for hypoglycemia. |
| **Risk with Sensors** | **Prevention and Mitigation** |

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|---|---|
| Risks with sensors may include:<br><br>• Skin irritation or reaction to adhesives<br>• Bruising<br>• Discomfort<br>• Redness<br>• Bleeding<br>• Pain<br>• Rash<br>• Infection<br>• Irritation from tapes used with glucose-sensing products<br>• Raised bump<br>• Appearance of a small "freckle-like" dot where needle was inserted<br>• Allergic reaction<br>• Syncopal episode secondary to needle insertion<br>• Soreness or tenderness<br>• Swelling at insertion site<br>• Sensor fracture, breakage or damage<br>• Minimal blood splatter associated with sensor needle removal<br>• Residual redness associated with adhesive and/ or tapes<br>• Scarring<br>• Scab<br>• Blister<br>• Itchiness<br>• Inflammation<br>• Anxiety<br>• Incorrect SG reading results in incorrect diabetes management<br>• Subject over-treating secondary to alarms which can result in hyperglycemia or hypoglycemia | Prevention and mitigation include:<br><br>• Follow the provided user guides for insertions and care of sensors.<br>• If a sensor site becomes infected or inflamed, the sensor will be removed and another sensor placed in a new location.<br>• 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.<br>• Instruct to check their meter glucose if there are any concerns that the SG value is not accurate.<br>• Instruct if there are no sensor values, no treatment decisions will be made until a BG is confirmed. |
| **Risks with Transmitter** | **Prevention and Mitigation** |
| Risks with transmitter may include:<br><br>• Skin irritation or reaction to adhesives<br>• Bruising<br>• Discomfort<br>• Redness<br>• Pain<br>• Rash<br>• Infection<br>• Irritation from tapes used with glucose-sensing products<br>• Raised bump | Prevention and mitigation include:<br><br>• Follow the provided user guides.<br>• Train on the proper use of the transmitters. |

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| • Allergic reaction<br>• Soreness or tenderness<br>• Residual redness associated with adhesive and/ or tapes<br>• Scarring<br>• Scab<br>• Blister<br>• Itchiness<br>• Inflammation | |
| **Risks with Serter** | **Prevention and Mitigation** |
| Risks with serters may include:<br><br>• Improper insertion may lead to device performance issue | Prevention and mitigation include:<br><br>• Follow the provided user guides for insertions and care of device.<br>• Train on the proper use of the serter and skin preparation prior to insertion. |
| **Risks with Fingersticks and Blood Draws** | **Prevention and Mitigation** |
| Risks with frequent fingerstick testing and blood draws may include:<br><br>• Potential risks associated with frequent meter testing of BG and blood ketones include discomfort and ecchymosis at tips of fingers<br>• Potential risks associated with fingerstick testing include discomfort and bruising<br>• Potential risks associated with drawing blood include discomfort, bruising and hematoma | Prevention and mitigation include:<br><br>• Follow the provided user guides for use of the study meter with fingerstick testing.<br>• Train on the proper use of the study meter and fingerstick testing.<br>• Blood draws will be performed by a trained healthcare professional |
| **Risk with Closed Loop Therapy** | **Prevention and Mitigation** |
| Risks with Closed Loop may include: | Prevention and mitigation include:<br><br>• Follow the provided user guides for insulin pump management.<br>• Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems.<br>• 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.<br>• Instruct to check their meter glucose if there are any concerns that the SG value is not accurate.<br>• Instruct if there are no sensor values, no treatments decision will be made until a BG is confirmed.<br>• Instruct to have glucose and glucagon on hand for hypoglycemia. |

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| • Hypoglycemia<br>• Severe hypoglycemia<br>• Hyperglycemia<br>• Diabetic ketoacidosis or HHS<br>• User entry error<br>  ○ Patient administering boluses by entering false carb doses leading to hypoglycemia or hyperglycemia<br>  ○ Patient entering false glucose values for any reason leading to hypoglycemia and hyperglycemia<br>  ○ Patient entering false BG values for calibration leading to hypoglycemia or hyperglycemia<br>• Sensor failure resulting from patient failure to calibrate leading to hypoglycemia or hyperglycemia<br>• Sensor over-reading resulting in hypoglycemia<br>• Sensor under-reading resulting in hyperglycemia<br>• Sensor missed transmission, or any other fault resulting in no SG value, leading to hyperglycemia or hypoglycemia<br>• 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<br>• Hypoglycemia related to patient taking insulin via injection while in Closed Loop (SmartGuard)<br>• Hypoglycemia or hyperglycemia related to entering or exiting Closed Loop (SmartGuard)<br>• Insulin over-delivery due to potential interference from acetaminophen<br>• Cyber security hacking into pump | • Instruct to avoid the use of products containing acetaminophen.<br>• If acetaminophen is taken, subjects will be instructed to use additional BG meter readings to verify their glucose levels.<br>• 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).<br>• Instruct subjects that in case of prolonged use of acetaminophen, the temp target feature can be used repeatedly and in succession.<br>• Pump has cybersecurity encryptions to prevent hacking. |
| Risks with hyperglycemia may include<br><br>• Diabetic ketoacidosis or HHS<br>• Symptomatic ketosis<br>• Cardiovascular event<br>• Dehydration<br>• Potassium and sodium imbalance<br>• Shock<br>• Altered mental status<br>• Coma<br>• Acidosis | Prevention and mitigation include:<br><br>• Follow the provided user guides for insulin pump management.<br>• Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems.<br>• 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.<br>• Instruct if there are no sensor values, no treatments decision will be made until a BG is confirmed. |
| Risks with hypoglycemia may include:<br><br>• Seizure<br>• Coma<br>• Altered mental status<br>• Loss of consciousness<br>• Cardiovascular event<br>• Death<br>• Risk of rebound hyperglycemia with ketosis | Prevention and mitigation include:<br><br>• Follow the provided user guides for insulin pump management.<br>• Train prior to study device use on appropriate device use and diabetes management principles and instruct to call investigator with problems.<br>• 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.<br>• Instruct to check their meter glucose if there are any concerns that the SG value is not accurate.<br>• Instruct if there are no sensor values, no treatment decisions will be made until a BG is confirmed.<br>• Instruct to have glucose and glucagon on hand for hypoglycemia. |
| **Risk with Acetaminophen Use** | **Prevention and Mitigation** |
| Potential risks with acetaminophen may include:<br><br>• 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<br>• Liver damage, liver failure and/or rare but fatal liver failure can occur<br>• Skin rash and/or serious and potentially fatal skin reactions have been reported<br>• Allergic reactions including those which are serious and potentially fatal can occur<br>• Kidney disease<br>• Lowered blood counts (red cells, and white cells) | Prevention and mitigation include:<br><br>• Follow the user guide.<br>• Instruct to avoid the use of products containing acetaminophen.<br>• If acetaminophen is taken, subjects will be instructed to use additional BG meter readings to verify their glucose levels.<br>• 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).<br>• Instruct subjects that in case of prolonged use of acetaminophen, the temp target feature can be used repeatedly and in succession. |

## 10.2 Risk Minimization

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

### 10.3 Potential Benefits

The main benefit of this study is that subjects may experience improved glucose control. 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. With all closed loop insulin pumps, there is a risk that the pump will deliver too much or not enough insulin, resulting in hypoglycemia or hyperglycemia. These risks have been minimized through previous characterization of the performance of the 780G system and a variety of safety checks that are an integral part of the 780G closed loop algorithm.

### 10.5 Risk Determination

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.[5]

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. [5]

**Severe Hyperglycemia** is defined as hyperglycemia (BG greater than [>] 300 mg/dL) 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, arterial pH less than (<) 7.3, bicarbonate less than (<) 15 mEq/L, moderate ketonuria or ketonemia and requiring treatment within a health care facility.[6]

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
- Serum ketones or large/moderate urine ketones
- Symptoms such as polyuria, polydipsia, nausea, or vomiting
- Treatment provided in a health care facility

**Hyperosmolar Hyperglycemic State/HHS diagnostic criteria:** BG greater than (>) 600 mg/dl, arterial pH greater than (>) 7.3, bicarbonate greater than (>) 15 mEq/l, minimal ketonuria and ketonemia and requiring treatment within a health care facility.[6]

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

- Arterial blood pH greater than (>) 7.3 or serum bicarbonate greater than (>) 15 mEq/L
- Blood glucose greater than (>) 600 mg/dL
- Negative/mild ketones
- 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.

## 11.3 Reporting of Adverse Events

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

Each AE needs to be assessed for its device or procedure relatedness. A device related AE is associated with the use of the study devices (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, HHS, 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, HHS, SAE, SADE, and UADE 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 upon request 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

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)). See **Section 12.20** for expedited reporting requirements for UADE.

The sponsor will notify the investigator and IRB of any event that results in a safety report per regulations to the FDA. Documentation of 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 IRB reporting requirements.***

## 11.6 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** |

### 11.7 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 or user guide.
- **Unanticipated:** the event has not been previously identified in the CIP; labeling; report of priors 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
- Severe hypoglycemia
- Diabetic ketoacidosis
- Diabetic hyperglycemic hyperosmolar syndrome
- Severe hyperglycemia

CEC is to review and adjudicate unanticipated adverse device effects (UADE), device related DKA, device related HHS, and device related severe hypoglycemia within 10 business days from the time that the sponsor is notified. Adjudication will occur once all applicable documentation has been

received and reviewed by the CEC.

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 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, HHS 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 HHS or 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, HHS 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, HHS 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, HHS 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 HHS
- 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:

- UADE

- Device related DKA
- Device related HHS
- Device related Severe Hypoglycemia

1. Investigational center staff will notify the sponsor within approximately 24 hours of investigator or study coordinator awareness of events described above.

2. Sponsor will notify the FDA within approximately 3 business days of awareness of the event and provide updates to the agency as information becomes available.

3. DMC is to meet within 10 business days from CEC adjudication of the event. The investigator should be available to answer questions from DMC, as needed.

4. Based on their review, DMC will recommend that the sponsor make a decision regarding the following:

   a) Whether or not subject enrollment may continue
   b) Whether or not new subject enrollment should be suspended, with enrolled subjects continuing in the study.
   c) Whether or not the entire study should be stopped, including those subjects who have already received study devices.

5. DMC and/or IRB will recommend whether or not the study should be stopped based on the number of events that have occurred during the study, weighed against the potential benefits of continuing the study.

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 provide a recommendation to proceed with the following staged enrollment:

After 10 subjects with a TDD at or below 125 units have completed 6 weeks of the study period, the DMC will assess if it is safe to proceed with subjects using SmartGuard who have a TDD of greater than 125 units.

**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.

# 13. Device Deficiencies and Troubleshooting

The Medtronic 24-Hour Technical Support (TS) will be consulted for device troubleshooting (e.g., assistance is needed by subject to operate their device[s]). When subjects call the TS, they are instructed to notify the TS operator that they are currently participating in a clinical research study. All device deficiencies that are reported to the TS will be documented by the TS staff.

The investigational center will be provided with a copy of all TS calls for their subjects. The TS call reports should be reviewed for investigational center staff awareness and assessment for the possibility of an AE. If an AE is detected the investigational center staff will complete the appropriate eCRF(s).

All device deficiencies reported directly to the investigational center staff by a subject should either be reported to the TS by the subject or investigational center staff. Any device deficiency the investigational center may have should be reported to the TS.

**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.

To return a study device as part of a device deficiency, the investigational center staff and/ or subject are required to call the 24-Hour TS. Following the call to TS, the investigational center staff should then follow the study procedures for returning products with device deficiencies.

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

# 14. Statistical Design and Methods

## 14.1 General Aspects of Analysis

For each phase, 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. For each phase, data and analyses 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

For each phase, 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 by period.

## 14.3 Subject Demographics and Baseline Characteristics

For each phase, 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.

## 14.4 Endpoints and Hypotheses

The following endpoints will be evaluated for each of the phases, separately.

**Phase 1:** MiniMed™ 780G insulin pump with Guardian 4 Sensor

**Phase 2:** MiniMed™ 780G BLE 2.0 insulin pump with DS5

### 14.4.1 Study Period

#### 14.4.1.1 Primary Safety Endpoint

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% with a margin of 0.4%. A significance level of 0.025 (one-sided) will be used.

The hypothesis of non-inferiority is mathematically expressed as:

$$H_0: \Delta\mu_{780G} \geq 0\% + 0.4\%$$

$$H_a: \Delta\mu_{780G} < 0\% + 0.4\%$$

**Note:** Phase 1 subjects transitioned into Phase 2 will not be included in this analysis for Phase 2.

#### 14.4.1.2 Primary Effectiveness Endpoint

The mean % of time in range (TIR 70-180 mg/dL), $\mu_{780G}$, will be estimated and compared by a non-inferiority test to the threshold of 70% with a margin of 7.5%. A significance level of 0.025 (one-sided) will be used.

The hypothesis of non-inferiority is mathematically expressed as:

$$H_0: \mu_{780G} \leq 70\% - 7.5\%$$
$$H_a: \mu_{780G} > 70\% - 7.5\%$$

#### 14.4.1.3 Secondary Effectiveness Endpoint

The mean % of time in range (TIR 70-180 mg/dL), $\mu_{780G}$, will be estimated and compared by a simple superiority test with a significance level of 0.025 (one-sided).

The hypothesis of superiority is mathematically expressed as:

$$H_0: \mu_{780G} \leq 70\%$$

$H_a$: $\mu_{780G} > 70\%$

[redacted]

#### 14.4.1.5 Device Deficiencies

Descriptive summary will be used to characterize device deficiencies:

- All reports of device issues.

#### 14.4.1.6 Subject Feedback

- Descriptive summary will be used to characterize study questionnaire results. Refer to CIP341 Questionnaire Guide for administration details.

#### 14.4.1.7 Safety Data Summarized

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

### 14.4.2 Run-in Period

#### 14.4.2.1 Device Deficiencies

Descriptive summary will be used to characterize device deficiencies:

- All reports of device issues.

#### 14.4.2.2 Subject Feedback

- Descriptive summary will be used to characterize study questionnaire results. Refer to CIP341 Questionnaire Guide for administration details.

#### 14.4.2.3 Safety Data Summarized

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

### 14.4.3 Continued Access Period

Only applicable for Phase 1.

#### 14.4.3.1 Device Deficiencies

Descriptive summary will be used to characterize device deficiencies:

- All reports of device issues.

#### 14.4.3.2 Safety Data Summarized

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

[redacted]

## 14.6 Study Reports

### 14.6.1 Phase 1

A study report will be generated once the subjects have completed the continued access period. Primary, secondary, and descriptive endpoints, subject feedback, and safety data for subjects will be summarized and presented in the report.

### 14.6.2 Phase 2

A study report will be generated once the subjects have completed the study period. Primary, secondary, and descriptive endpoints, subject feedback, and safety data for subjects will be summarized and presented in the report.

# 15. Ethics

## 15.1 Statement(s) of Compliance

This clinical study will be conducted in compliance with the CIP, Clinical Investigation Agreement; US CFR Title 21 Part 11 (Electronic Records; Electronic Signatures), Part 50 (Informed consents), Part 54 (Financial Disclosure by Clinical Investigators), Part 56 (IRBs), Part 812 (Investigational Device Exemptions), and all other applicable federal and local regulatory requirements.

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

The ethical principles that have their origin in the Declaration of Helsinki (DoH) have been implemented in this clinical study by means of the informed consent process, IRB approval, study training, clinical trial registration, pre-clinical testing, risk-benefit assessment, publication policy, etc.

## 15.2 IRB Approval

This CIP, any subsequent amendments to this CIP, the ICF form, subject materials, and any form of subject recruitment information (e.g., advertisements) relating to this study will be approved by the responsible IRB in accordance with 21 CFR Part 56.

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

## 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." Each investigational center shall designate a primary

investigator who will have overall responsibility for the conduct of the investigation at the investigational center.

The principal investigators (and co-investigators if applicable) are responsible for conducting the study in accordance with this CIP, CTA, and 21 CFR Part 812 that apply to significant risk (SR) device studies. 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", 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 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 (21 CFR 812.100)

- Providing adequate supervision of those to whom tasks have been delegated. The investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of a clinical study.

- Ensuring that the requirements for obtaining informed consent are met in accordance with 21 CFR 50

- 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 under 21 CFR Part 812 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 (21 CFR 812.140), to include:
    - attribution, legibility, and timeliness of source data
    - all relevant correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, 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 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 and the reviewing 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 and 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
    - any further information requested by the FDA and 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 (21 CFR 812.145)
- 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 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, IRB review, and regulatory inspections.

### 16.2.3 Investigational Center Disqualification

Sponsor and/or the 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 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 subject'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 Subject Questionnaires

In this study, we are collecting subject feedback regarding user experience and quality of life through questionnaires. Subjects will be provided a link to complete the questionnaires that will be kept online. Refer to CIP341 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

Subjects will be paid for participation. Refer to the ICF on the details of the subject's compensation.

## 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 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 IRB. Administrative amendments to the CIP will be submitted to the IRB for notification.

## 16.8 Records and Reports

### 16.8.1 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
- Report of prior investigations and/or user guide
- Medtronic and IRB-approved Subject ICF form
- 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 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

### 16.8.2 Investigator Reporting Responsibilities

**Table 5. Investigator Reporting Requirements**

| Report | Submit to | Description/Constraints |
|---|---|---|
| AEs and DDs | Sponsor, IRB, and regulatory authority, where applicable | Refer to **Section 11** and **13** for reporting requirements. |
| 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 prior to investigational device use | Sponsor and IRBs | If an investigator uses a device without obtaining informed consent the investigator shall report such use within 5 working days after device use. |
| Final report | Sponsor<br>IRBs<br>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. |

## 16.9 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.

## 16.10 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 authority of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform the reviewing IRB and the study subjects.

### 16.10.1 Early Investigational Center Suspension or Termination

Sponsor, 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 IRB, non-compliance to the CIP, or lack of enrollment). Suspended clinical studies cannot be resumed without permission from 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 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 IRB, if applicable.

### 16.10.2 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.

## 16.11 Study Close-Out

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

## 16.12 Publication and Use of Information

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. Inzucchi, S.E. and R.S. Sherwin, *The prevention of type 2 diabetes mellitus.* Endocrinol Metab Clin North Am, 2005. **34**(1): p. 199-219, viii.
2. Jack, L., Jr., L. Boseman, and F. Vinicor, *Aging Americans and diabetes. A public health and clinical response.* Geriatrics, 2004. **59**(4): p. 14-7.
3. Centers for Disease, C. and Prevention, *Prevalence of overweight and obesity among adults with diagnosed diabetes--United States, 1988-1994 and 1999-2002.* MMWR Morb Mortal Wkly Rep, 2004. **53**(45): p. 1066-8.
4. Reznik, Y., et al., *Insulin pump treatment compared with multiple daily injections for treatment of type 2 diabetes (OpT2mise): a randomised open-label controlled trial.* Lancet, 2014. **384**(9950): p. 1265-72.
5. Cryer, P.E., *Defining and reporting hypoglycemia in diabetes: A report from the American diabetes association workgroup on hypoglycemia.* Diabetes Care, 2005. **28**(5): p. 1245-1249.
6. *Hyperglycemic Crises in Diabetes.* Diabetes Care, 2004. **27**(SUPPL. 1): p. S94-S102.

# 18. Appendices

## 18.1 Appendix 1: Names and addresses

### 18.1.1 Investigational Centers and 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]
[redacted]
Medtronic
710 Medtronic Parkway
Minneapolis, MN 55432

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

## 18.2 Appendix 2: Labeling of Devices

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

## 18.3 Appendix 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, and the HIPAA Authorization.

## 18.4 Appendix 4: Phase 1 – This phase has been completed

Phase 1 has been completed and subjects are no longer being enrolled in or participating in this phase of the study.

### 18.4.1 Study Design

Phase 1 will study the MiniMed™ 780G insulin pump with Guardian 4 Sensor. The period from Visit 1 (consent and screening) through Visit 8 should be completed within 45 days.

**Run-in Period (Visits 2-8):**

The run-in period begins at Visit 2 and ends once Visit 9 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, Humalog (insulin lispro injection), NovoLog/NovoRapid (insulin aspart solution for injection), or Admelog (insulin lispro injection).

During the run-in period of the study, subjects will be using the study pump in Manual Mode, with only the Sensor Augmented Pump (SAP) function activated (i.e., SmartGuard feature turned OFF). The "Suspend before Low" and "Suspend on Low" features may be used.

| Therapy at Screening | Pump Setting During Run-in Period |
|---|---|
| Continuous Subcutaneous Insulin Infusion (CSII) | Manual Mode |
| SAP (no closed loop) | Manual Mode |
| SAP (with closed loop [i.e., AID]) in non-Medtronic pump | Manual Mode |
| SAP (with closed loop) in Medtronic pump as Auto Mode | SmartGuard feature with Auto Correction OFF |

All subjects will be trained on diabetes management principles, such as the treatment of hyperglycemia and hypoglycemia. In addition, there will be training by investigational center staff regarding the need to have access to and how to use glucose and glucagon in case of hypoglycemia.

Companions/care partners will be instructed that they should be with the subject in the same residence or building complex overnight.

If the MiniMed Clinical app and the Carelink Clinical app are being used, companions/care partners 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 work, other activities. Instructions on the appropriate operation of the apps will be provided.

For study purposes, subjects will be instructed to perform self-monitoring of blood glucose (SMBG) if they are experiencing a severe hypoglycemic event, severe hyperglycemic event, hyperglycemic hyperosmolar syndrome (HHS), or diabetic ketoacidosis (DKA).

Blood ketones will be measured by all subjects using a ketone meter when:

- the subject is symptomatic for high blood glucose or
- the sensor glucose value is >300mg/dL, the BG is checked by fingerstick and, if BG is >300mg/dL, blood ketones should be checked

As a precaution, subjects 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 device issues (e.g., infusion set occlusion with high glucose).

Subjects will be instructed to insert study sensors only in the locations that are specified in the User Guide. Subjects should be reminded about appropriate study sensor placement at each office visit. Information about predominant location of study sensor insertions will be collected on an electronic case report form (eCRF) at the end of a subject's participation.

Subjects will be trained on all parts of the device system. Companions/care partners should be trained on how to respond to high or low glucose events. This should involve training conducted by investigational center staff. A training checklist for each subject should be completed by investigational center-based trainers. Companions/care partners should be available for relevant parts or, if desired, all of this training, either in person or virtually.

After completion of training on the study devices, subjects will be asked to attend additional visits in the days immediately following the start of system use, as needed. They may also take advantage of having continued access to the digital learning content, provided it is available at study start.

**Study Period (Visits 9-18):**
The study period begins at Visit 9 and ends at the conclusion of Visit 18.

Subjects will continue using the study pump and study sensor and will use the SmartGuard feature for approximately 90 days during the study period. Subjects should use the system with the SmartGuard feature (with Auto Correction ON) turned on at all times. When prompted by the pump, subjects should take appropriate measures and follow directions on the pump to remain in, or return to, SmartGuard. During times when subjects are not able to use SmartGuard, they should use the system in Manual Mode (e.g., using Suspend before low and Suspend on low settings).

**Pump Settings:**
During the first 3 weeks (between Visits 9 and 14) of the study period, a 120 mg/dL 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 at the investigator's discretion.

During the next 3 weeks (between Visits 14 and 16) of the study period, a 100 mg/dL Auto Basal Target should be set. Active Insulin time is recommended to be set to 2-3 hours or at investigator's discretion.

During the remaining weeks (any time after Visit 16) 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 discretion.
The Auto Basal target setting and Active Insulin Time should be set as shown above unless there is a documented safety reason that would not permit these settings to be used.

After completion of training on SmartGuard functions, subjects 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 digital learning content, provided it is available at study start.

**SMBG recommendations for 780G system:**
With the 780G system and the study sensor, calibration is not required. However, a calibration is optional, and it will automatically 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 SmartGuard. 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 periods.

- 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.

It is important for subjects to avoid additional meal/snack or exercise up to 4 hours after the start of each challenge. If additional meal/snack is consumed or exercise is done within 4 hours after the start of the challenge, the subject will acknowledge this on the challenge log. Subjects will be asked to check BG at the start of the meal/exercise, as well as 2 hours and 4 hours after the meal/exercise and take bolus correction as necessary. Content and timing of the meal and exercise, along with answers to challenge questions, 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 (between visits 7 and 9) with subjects using the system in **Manual Mode** (SmartGuard must be turned off at least 6 hours prior to the meal challenge for subjects using it during the run-in period)
  - One Regular sized meal with ***missed meal bolus*** at lunch
  - One Large sized meal at breakfast, lunch or dinner

- Two meal challenges during the study period (between Visits 12 and 14) with subjects using the system in SmartGuard, Auto Basal target set at 120 mg/dL
  - One Regular sized meal with ***missed meal bolus*** at lunch
  - One Large sized meal at breakfast, lunch or dinner

- Two meal challenges during the study period (between Visits 15 and 16) with subjects using the system in SmartGuard, Auto Basal target set at 100 mg/dL
  - One Regular sized meal with ***missed meal bolus*** at lunch
  - One 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 investigator's discretion – at any time after Visit 16
  - One 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
- Sensor glucose is available.

| Timing | Settings/Conditions | Meal Size | Meal Type | Notes |
|---|---|---|---|---|
| **Run-in Period between visits 7 and 9** | 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 7 and 9** | 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 12 and 14** | SmartGuard (120 mg/dL 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 setpoint |

| | | | | |
|---|---|---|---|---|
| **Study Period between Visits 12 and 14** | SmartGuard (120 mg/dL 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 and run-in period meal |
| **Study Period between Visits 15 and 16** | SmartGuard (100 mg/dL 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. |
| **Study Period between Visits 15 and 16** | SmartGuard (100 mg/dL 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 and run-in period large sized meal |
| **Study Period Any time after Visit 16** | SmartGuard (Auto Basal target setpoint at investigator's discretion) | 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 /100mg/dL and run-in period large sized meals |

**Details about Regular Meal Challenges 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 patients would normally eat at this mealtime. Subjects will be asked to check BG at the start of the meal, as well as 2 hours and 4 hours after the meal and provide correction as necessary. Content and timing of the meal, along with BG values, will be recorded on a log provided by the study team.

During the study period, once at each Auto Basal setpoint (i.e. 120 mg/dL and 100 md/dL), 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. Subjects will be asked to check BG at the start of the meal, as well as 2 hours and 4 hours after the start of the meal and provide correction as necessary. Details should be recorded, along with BG values, on the log.

**Details about Large sized Meal Challenges:**

On large sized meal challenge days, subjects will be instructed to eat one 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. A log will be used to collect information about the food that was eaten, the name of the restaurant (if applicable), and confirmation that meal size was at least 50% more in terms of calories, carbohydrates and fat. The log will also be used to record the time and date of the meal and check box confirmation that a BG was taken at the start of the meal, 2 hours after the start of the meal and 4 hours after the start of the meal. The timing of the meal challenges will be at the investigator's discretion. The subject's

companion/care partner 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). They must be able to check SMBG (in case it is needed) and give glucose/administer glucagon if required.

**Exercise Challenge for all subjects (during Study Period only):**

The following exercise challenges are required during the study period:

- 2 exercise challenges at setpoint of 120 mg/dL, between Visits 12 and 14
- 2 exercise challenges at setpoint of 100 mg/dL, between Visits 15 and 16
- 1 exercise challenge at investigator's discretion, at any time after Visit 16

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 12 and 14** | SmartGuard (120 mg/dL setpoint) | Min 30 minutes, up to 1.5 hours | Challenge must take place on days without meal challenge |
| **Study Period between Visits 12 and 14** | SmartGuard (120 mg/dL setpoint) | Min 30 minutes, up to 1.5 hours | Challenge must take place on days without meal challenge |
| **Study Period between Visits 15 and 16** | SmartGuard (100 mg/dL setpoint) | Min 30 minutes, up to 1.5 hours | Challenge must take place on days without meal challenge |
| **Study Period between Visits 15 and 16** | SmartGuard (100 mg/dL setpoint) | Min 30 minutes, up to 1.5 hours | Challenge must take place on days without meal challenge |
| **Study Period Any time after Visit 16** | SmartGuard (Auto Basal target setpoint at investigator's discretion) | 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 or 120 mg/dL, depending on what is required at that time of the study period, unless a subject prefers to use the 150 mg/dL temp target before, during and immediately after the exercise challenges. A log will be used to collect information about exercise type, date, time (start and finish of exercise) and duration. The log should also ask a confirmation that SMBG was done at the

beginning of exercise, as well as 2 and 4 hours after the start of the exercise. 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. The subject's companion/care partner 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.

Subjects should have carbohydrates available during and after exercise, if needed for safety reasons.

If, during exercise, subjects experience any physical discomfort (e.g., chest pain, palpitations, shortness of breath, dizziness), exercise should be stopped immediately and subject should seek medical attention, if required. Subjects should contact the investigational center to report incidences of discomfort that lead to the cessation of exercise.

Examples of types of exercise include, but are not limited to:

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

**Companions:**
Subjects will be required to have a companion (may be care partner) 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 (Phase 1). Companions should be able to check SMBG, give glucose and/or administer glucagon.

**Continued Access Period (from the end of Visit 18):**
Phase 1 subjects will have the opportunity to transition into Phase 2 upon completion of Phase 1 – Study Period or at their next continued access period visit. The continued access period for Phase 1 of the study will end as soon as subjects transition to Phase 2 or exit the study.

### 18.4.2 Study Visit Schedule

Subjects will participate in a minimum of 18 planned study visits, as presented below in

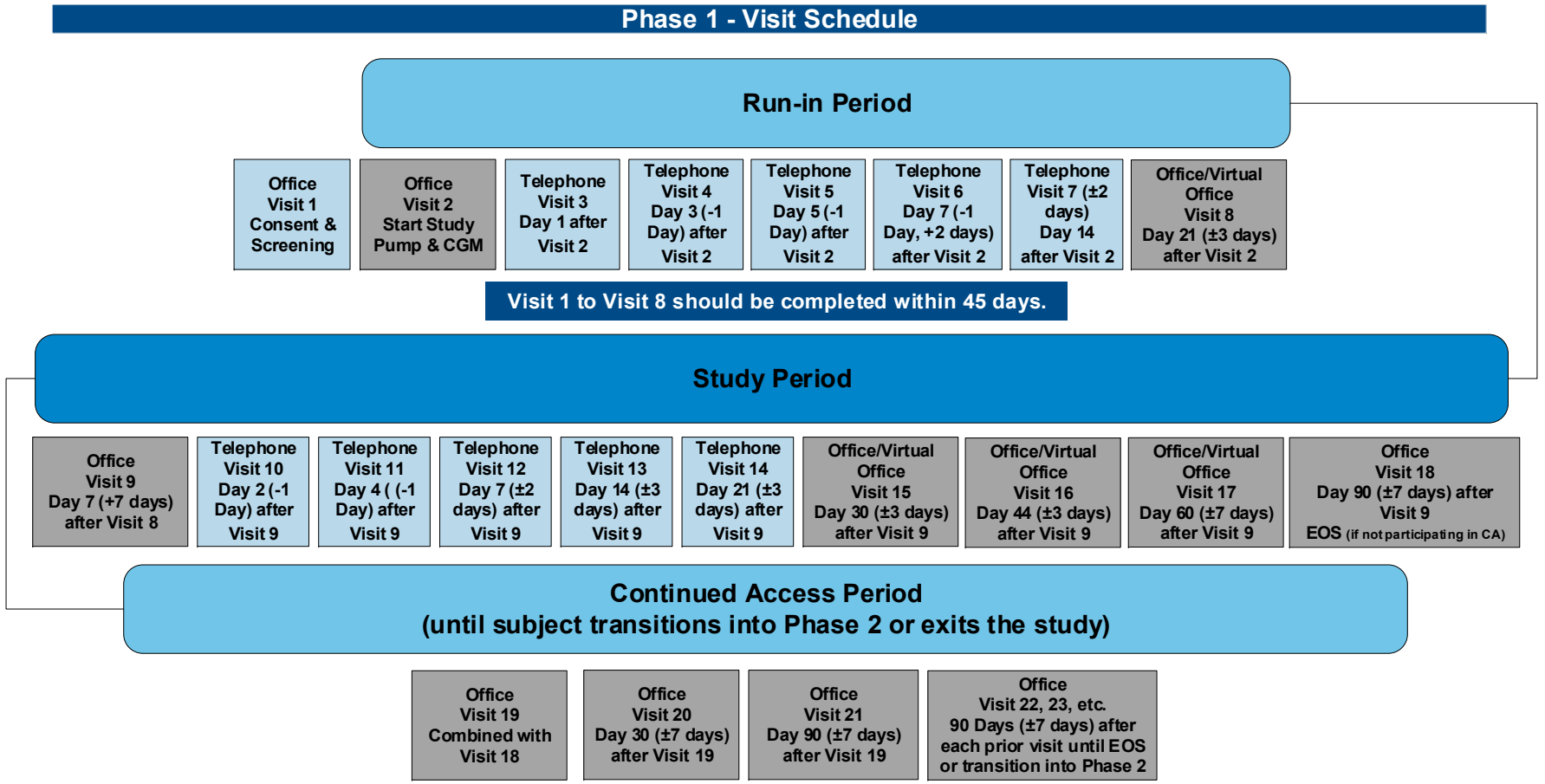
**Figure** 7, for approximately 135 days of device wear. Subjects may enter a continued access period, following the end of the study period. Virtual office visit (audio visual) may be performed for office visits in cases where an office visit is not possible. The exit visit should occur at the office 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.

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 9. Refer to CIP341 Questionnaire Guide for collection of early exit survey/questionnaire requirements.

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

**Figure 7. Phase 1 Visit Schedule – This phase has been completed**



**Visit 1 to Visit 8 should be completed within 45 days.**

- Visit 1 (Office): Consent and screening
  - Collect labs

**Run-In Period:**

- Visit 2 (Office): Start Run-In
  - Eligibility has been confirmed
  - Start study pump and CGM in Manual Mode
  - Register and upload study pump in CareLink Personal and CareLink system
  - Ask subjects about adverse events and device performance

- Visit 3 (Phone): Day 1 after Visit 2
  - Ask subjects if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 4 (Phone): Day 3 (-1 day) after Visit 2
  - Ask subjects if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 5 (Phone): Day 5 (-1 day) after Visit 2
  - Ask subjects if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 6 (Phone): Day 7 (-1, +2 days) after Visit 2
  - Ask subjects if they require assistance, e.g., additional training
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Visit 7 (Phone): Day 14 (±2 days) after Visit 2
  - Ask subjects if they required 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 8 (Office/Virtual Office): Day 21 (±3 days) after Visit 2
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

**Study Period:**

- Visit 9 (Office): Start Study Period, Day 7 (+7) after Visit 8
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Start subjects on SmartGuard
  - Start auto basal target at 120 mg/dL
  - Instruct subjects about the required meal and exercise challenges for the 120 mg/dL and 100 mg/dL setpoint during the study period

- Visit 10 (Phone): Day 2 (-1 day) after Visit 9
  - Adjust pump settings as needed
  - Ask subjects 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 setpoint

- Visit 11 (Phone): Day 4 (-1 day) after Visit 9
  - Adjust pump settings as needed
  - Ask subjects 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 setpoint

- Visit 12 (Phone): Day 7 (±2 days) after Visit 9
  - 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 setpoint

- Visit 13 (Phone): Day 14 (±3 days) after Visit 9
  - 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 setpoint

- Visit 14 (Phone): Day 21 (±3 days) after Visit 9
  - Adjust pump settings as needed
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Change auto basal target at 100 mg/dL setpoint
  - Remind subjects about meal/exercise challenges for 100 mg/dL setpoint

- Visit 15 (Office/Virtual Office): Day 30 (±3 days) after Visit 9
  - Adjust pump settings as needed
  - Ask subjects about adverse events and device performance
  - Review CareLink reports

- Remind subjects about meal/exercise challenges for 100 mg/dL setpoint

- Visit 16 (Office/Virtual Office): Day 44 (±3 days) after Visit 9
  - 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 17 (Office/Virtual Office): Day 60 (±7 days) after Visit 9
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Remind subjects about meal/exercise challenges

- Visit 18 (Office): Day 90 (±7 days) after Visit 9
  - Collect HbA1C
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Return study devices – unless subject decides to enter continued access period
  - End of Study (EOS) – unless subject decides to enter continued access period
  - Will be combined with Visit 19 if subject decides to enter continued access period

**Continued Access Period:** Phase 1 subjects will have the opportunity to transition into Phase 2 upon completion of Phase 1 – Study Period or at their next continued access period visit. The continued access period for Phase 1 of the study will end as soon as subjects transition to Phase 2 or exit the study.

- Visit 19 (Office): Combined with Visit 18
  - Subjects are instructed to continue uploading study device data at least weekly
  - Instruct subjects about the use of SGLT inhibitors

- Visit 20 (Office): Day 30 (±7 days) after Visit 19
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Remind subjects about the use of SGLT inhibitors

- Visit 21 (Office): Day 90 (±7 days) after Visit 19
  - Ask subjects about adverse events and device performance
  - Review CareLink reports
  - Collect HbA1c
  - Remind subjects about the use of SGLT inhibitors
- Subsequent visits (Visit 22, 23, etc.) will take place at 90-day intervals (±7 days) from Visit 21 (with the same questions asked and collection of HbA1c as during Visit 21), until the Sponsor announces the end of the study. The continued access visits should be Office visits, barring circumstances that put patient safety at risk (e.g., events

related to COVID-19), or where in person visits may not be allowed. HbA1c should be collected every 90 days. If a subject elects to leave the study at any point during the continued access period, devices will be collected at that time and study exit procedures will be followed.

### 18.4.3 Study Visit Details

| | | Run-In Period | | | | | Study Period | | | | | | Continued Access Period | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Visit 1 (Office) | Visit 2 (Office) | Visit 3, 4 & 5 (Phone) | Visit 6 (Phone) | Visit 7 (Phone) | Visit 8 (Office/ Virtual Office) | Visit 9 (Office) | Visit 10 & 11 (Phone) | Visit 12, 13 & 14 (Phone) | Visit 15 & 16 (Office/ Virtual Office) | Visit 17 (Office/ Virtual Office) | Visit 18* (Office) | Visit 19 (Office) | Visit 20 (Office **) | Visit 21 (Office **) | Visits 22, 23, etc. (Office **) |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 EOS Period** | **Combined with Visit 18** | **Day 30 (±7 days) after Visit 19** | **Day 90 (±7 days) after Visit 19** | **90 Days (±7 days) after each prior visit** |
| **Visit Activities and Data Collection** | | | | | | | | | | | | | | | | |
| Collect consent forms, e.g., ICF, 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<br>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. All collected blood specimens will be sent to and tested by a NGSP certified Central Laboratory. Testing must follow NGSP standards.<br>Note: If the visit must be conducted via Virtual Office, the blood tests may be collected via mobile phlebotomy service. | X | | | | | | | | | | | X | | | X (if applicable) | X (if applicable) |
| Collect specimens for required local lab testing: Hematocrit, Creatinine, TSH, GAD, c-peptide (Note: | X | | | | | | | | | | | | | | | |

| | | Run-In Period | | | | | Study Period | | | | | | Continued Access Period | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/ Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/ Virtual Office)** | **Visit 18* (Office)** | **Visit 19 (Office)** | **Visit 20 (Office **)** | **Visit 21 (Office **)** | **Visits 22, 23, etc. (Office **)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 EOS Period** | **Combined with Visit 18** | **Day 30 (±7 days) after Visit 19** | **Day 90 (±7 days) after Visit 19** | **90 Days (±7 days) after each prior visit** |
| c-peptide is not part of inclusion/exclusion criteria) – see lab instructions for additional information | | | | | | | | | | | | | | | | |
| Collect information about medical history | X | | | | | | | | | | | | | | | |
| Collect information about concomitant medications | X | | | | | | | | | | | | | | | |
| Collect any changes to diabetes medications during the study (including the type of insulin being used). The only insulins permitted for use in the study are Humalog, Novolog/NovoRapid, and Admelog. | | 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) | 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 CIP341 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 | 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 | As needed | As needed |
| Train subjects on the use of the Accu-Chek Guide Link study meter and ketone meter, refer to user guides | | X | | | | | | | | | | | | | | |
| Train subjects on the use of the 780G pump with Guardian 4 sensor | | X | | | | | | | | | | | | | | |
| Start study subjects on the 780G insulin pump system (Manual Mode) | | X | | | | | | | | | | | | | | |
| Provide study subjects the Medtronic infusion sets, reservoirs, sensors and transmitter | | X | | | | As needed | As needed | | | As needed | As needed | As needed | As needed | As needed | As needed | As needed |
| Train subjects on the Medtronic infusion sets, reservoirs, sensors and transmitter | | X | | | | | | | | | | | | | | |

| | | Run-In Period | | | | | Study Period | | | | | | Continued Access Period | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/ Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/ Virtual Office)** | **Visit 18* (Office)** | **Visit 19 (Office)** | **Visit 20 (Office **)** | **Visit 21 (Office **)** | **Visits 22, 23, etc. (Office **)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 EOS Period** | **Combined with Visit 18** | **Day 30 (±7 days) after Visit 19** | **Day 90 (±7 days) after Visit 19** | **90 Days (±7 days) after each prior visit** |
| Start study subjects on CGM (transmitter and sensor) and accessories | | X | | | | | | | | | | | | | | |
| Instruct subjects 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 | If applicable | X | X | X | X |
| Train study subjects on the 780G SmartGuard features. | | | | | | | X | | | | | | | | | |
| Instruct subjects on the SmartGuard feature of the pump as well as specific considerations regarding SmartGuard:<br>• Ensure that the Auto Correction feature is turned ON and remains ON throughout the course of the study.<br><br>Instruct subjects to switch from pump therapy to manual injections until issue is resolved if:<br>• Hospital admission is needed for any reason<br>• Glucose is persistently elevated (i.e., above 300 mg/dL) and not responding to correction boluses and/or infusion set change(s).<br>• There is an occlusion alarm with elevated glucose, where the study subject is not able to address the occlusion by changing the infusion set | | | | | | | X | | | | | | | | | |
| Adjust pump settings | | X | As needed | As needed | As needed | As needed | X | As needed | As needed | As needed | As needed | As needed | As needed | As needed | 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 | | | | | | | | | | | | | | |

| | | Run-In Period | | | | | Study Period | | | | | | Continued Access Period | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/ Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/ Virtual Office)** | **Visit 18* (Office)** | **Visit 19 (Office)** | **Visit 20 (Office **)** | **Visit 21 (Office **)** | **Visits 22, 23, etc. (Office **)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 EOS Period** | **Combined with Visit 18** | **Day 30 (±7 days) after Visit 19** | **Day 90 (±7 days) after Visit 19** | **90 Days (±7 days) after each prior visit** |
| Link the study subjects account to the investigational center account | | X | | | | | | | | | | | | | | |
| Train subjects on the use of CareLink Personal– provide relevant set of written instructions | | X | | | | | | | | | | | | | | |
| Set up 780G system apps, if applicable:<br>• MiniMed Clinical app<br>• CareLink Clinical app | | X | | | | | | | | | | | | | | |
| If applicable:<br>Train subjects and companions/care partners on the use of the 780G system apps: MiniMed Clinical app and CareLink Clinical app | | X (if applicable) | | X (if applicable) | | X (if needed) | | | | | | | | | | |
| If applicable:<br>For subjects who are currently using SGLT inhibitors, the investigational center will provide training as well as a wallet card-formatted STICH protocol. | | 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) | X (if applicable) | X (if applicable) | X (if applicable) | X (if applicable) |
| Instruct/Remind subjects and their companions/care partners about the requirement to perform meal challenges during the run-in period<br>SmartGuard should not be activated.<br>Instruct subjects about the Smartphone app to collect meal data. | | | | X | | | | | | | | | | | | |
| Instruct/Remind subjects about the requirement to perform meal and exercise challenges during the study period:<br>• At 120 mg/dL Auto Basal Setpoint **Week 2-3** of the study period<br>• At 100 mg/dL Auto Basal Setpoint during **Week 5 -6** of the study period<br>• At current Auto Basal Setpoint anytime after **Week 6** of the study period | | | | | | | X | X | X | X | | | | | | |

| | | Run-In Period | | | | | Study Period | | | | | | Continued Access Period | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Visit 1 (Office) | Visit 2 (Office) | Visit 3, 4 & 5 (Phone) | Visit 6 (Phone) | Visit 7 (Phone) | Visit 8 (Office/ Virtual Office) | Visit 9 (Office) | Visit 10 & 11 (Phone) | Visit 12, 13 & 14 (Phone) | Visit 15 & 16 (Office/ Virtual Office) | Visit 17 (Office/ Virtual Office) | Visit 18* (Office) | Visit 19 (Office) | Visit 20 (Office **) | Visit 21 (Office **) | Visits 22, 23, etc. (Office **) |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 EOS Period** | **Combined with Visit 18** | **Day 30 (±7 days) after Visit 19** | **Day 90 (±7 days) after Visit 19** | **90 Days (±7 days) after each prior visit** |
| Advise subjects that they should contact the investigational center staff if they develop symptoms during the exercise that prompt them to stop, e.g., chest pain, palpitations, shortness of breath, dizziness<br>Instruct subjects about the Smartphone app to collect meal and exercise data. | | | | | | | | | | | | | | | | |
| Start Auto Basal Target = 120 mg/dL with Active Insulin Time = 4 hours-titrated towards 2-3 hours at investigator's discretion at Visit 9 | | | | | | | X | | | | | | | | | |
| Start Auto Basal Target = 100 mg/dL with Active Insulin Time = 2-3 hours or at investigator's discretion at Visit 14 | | | | | | | | | X (Visit 14) | | | | | | | |
| Dispense study materials (e.g., smartphone [upon request and approval], reference guides, subject training materials, etc.) | | X | | | | | X | X | X | | | | | | | |
| Dispense other study supplies as needed (e.g., alcohol swabs, adhesive remover, etc.) | | X | | | | As needed | As needed | | | As needed | As needed | As needed | 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 | 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 | X | X |
| Review CareLink system reports | | | X | | | X | X | X | | X | X | If applicable | 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 | As needed | As needed | As needed |
| Enter data into eCRFs as required | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |

| | | Run-In Period | | | | | Study Period | | | | | | Continued Access Period | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/ Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/ Virtual Office)** | **Visit 18* (Office)** | **Visit 19 (Office)** | **Visit 20 (Office **)** | **Visit 21 (Office **)** | **Visits 22, 23, etc. (Office **)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 EOS Period** | **Combined with Visit 18** | **Day 30 (±7 days) after Visit 19** | **Day 90 (±7 days) after Visit 19** | **90 Days (±7 days) after each prior visit** |
| Schedule next visit day and time | X | X | X | X | X | X | X | X | X | X | X | If applicable | | | | |
| Collect study devices at study end (see device disposition **Table 2** for details).<br>Note: If the visit must be conducted via Virtual Office, the blood tests may be collected via mobile phlebotomy service. Subjects should send devices back to the investigational center. | | | | | | | | | | | | If EOS | | | | When subject exits or sponsor concludes study |
| **Questions To Ask at Study Visits** | | | | | | | | | | | | | | | | |
| Ask if subjects have general study-related questions and concerns | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Ask subjects about the occurrence of adverse events.<br>• 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<br>• 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 | X | X | X | X |
| Ask subjects about device performance issues and if they called the Medtronic 24 -Hour Technical Support (TS) line to report them.<br>Instruct/Remind subjects to contact the Medtronic 24-Hour TS in the event they experience problems with their study devices. | | X | X | X | X | X | X | X | X | X | X | X | X | X | X | X |
| Ask subjects if they require assistance, e.g., additional training | | | X | X | X | X | | X | | | | | | | | |

| | | Run-In Period | | | | | Study Period | | | | | | Continued Access Period | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **Visit 1 (Office)** | **Visit 2 (Office)** | **Visit 3, 4 & 5 (Phone)** | **Visit 6 (Phone)** | **Visit 7 (Phone)** | **Visit 8 (Office/ Virtual Office)** | **Visit 9 (Office)** | **Visit 10 & 11 (Phone)** | **Visit 12, 13 & 14 (Phone)** | **Visit 15 & 16 (Office/ Virtual Office)** | **Visit 17 (Office/ Virtual Office)** | **Visit 18* (Office)** | **Visit 19 (Office)** | **Visit 20 (Office **)** | **Visit 21 (Office **)** | **Visits 22, 23, etc. (Office **)** |
| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 EOS Period** | **Combined with Visit 18** | **Day 30 (±7 days) after Visit 19** | **Day 90 (±7 days) after Visit 19** | **90 Days (±7 days) after each prior visit** |
| Ask subjects about the use of SGLT inhibitors during the Continued Access Period | | | | | | | | | | | | | X | X | X | X |
| **Study Subject General Training and Instructions** | | | | | | | | | | | | | | | | |
| Remind subjects that the use and wear of study devices throughout the study is a requirement | | X | X | X | X | X | X | X | X | X | X | If applicable | X | X | X | X |
| Instruct/Remind subjects regarding the content of the Home Reference Guide | | X | | | | | | | | | | | X | | | |
| Instruct subjects on carbohydrate (CHO) counting as needed (Investigator discretion) | | X | X | X | X | X | X | X | X | X | X | If applicable | X | X | X | |
| Instruct subjects on diabetes self-management principles including response to glycemic events, e.g., use of oral glucose/glucagon in case of severe hypoglycemia or checking for ketones in case of severe hyperglycemia<br>Note: Companions/care partners should be trained on how to respond to high or low glucose events. | | X | | | | | | | | | | | | | | |
| Instruct subjects and companions/care partners that blood ketone testing is required every time BG is greater than 300 mg/dL, as measured by the Accu-Chek Guide Link study meter. | | X | X | X | X | X | X | X | X | X | X | If applicable | X | X | X | X |
| Instruct subjects to consider avoiding the use of products containing acetaminophen.<br>If medications containing acetaminophen are taken:<br>• Wait until use of the medication is stopped before using SG to make treatment decisions<br>• Use additional BG meter readings to verify glucose levels<br>• While the SmartGuard feature is active, instruct subjects to use the temp target | | X | X | X | X | X | X | X | X | X | X | If applicable | X | X | X | X |

| | | Run-In Period | | | | | Study Period | | | | | | Continued Access Period | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
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| **Visit Window** | **Enrollment** | | **Day 1, 3 (-1 day), and 5 (-1 day) after Visit 2** | **Day 7 (-1 day, +2 days) after Visit 2** | **Day 14 (±2 days) after Visit 2** | **Day 21 (±3 days) after Visit 2** | **Day 7 (+7 days) after Visit 8** | **Day 2 (-1 day) and 4 (-1 day) after Visit 9** | **Day 7 (±2 days), 14 (±3 days), and 21 (±3 days) after Visit 9** | **Day 30 (±3 days) and 44 (±3 days) after Visit 9** | **Day 60 (±7 days) after Visit 9** | **Day 90 (±7 days) after Visit 9 EOS Period** | **Combined with Visit 18** | **Day 30 (±7 days) after Visit 19** | **Day 90 (±7 days) after Visit 19** | **90 Days (±7 days) after each prior visit** |
| feature (when used, Auto Correction is not available)<br>• Instruct subjects that in case of prolonged use of acetaminophen, the temp target feature can be used repeatedly and in succession | | | | | | | | | | | | | | | | |
| Remind subject to bring in both Accu-Chek Guide Link study meter and ketone meter at each required office visit. | | X | | | X | X | | | X | X | X | If applicable | X | X | X | X |
| Remind subject to keep their devices charged, as applicable | | X | X | | | X | X | X | | X | X | If applicable | X | X | X | X |
| Instruct subjects regarding the use of the Accu-Chek Guide Link study meter to make treatment decisions:<br>• When a BG required alert is received:<br>○ Clear the alert and enter a BG meter reading before using the SG to make treatment decisions<br>• When symptoms are present:<br>○ If SG readings are not aligned with symptoms (e.g., if a study subject is feeling low while the SG reading is not low), use the meter to confirm BG.<br>○ If SG readings continue to be different from symptoms, call the study doctor | | X | X | | | X | X | X | | X | X | If applicable | X | X | X | X |
| Instruct subjects 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 | X | X | X | X |
| Instruct subjects that they should not assume that SmartGuard is able to prevent all hypoglycemia or all | | X | | | | | X | | | X | X | If applicable | X | X | X | X |

| | | Run-In Period | | | | | Study Period | | | | | | Continued Access Period | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Visit 1 (Office) | Visit 2 (Office) | Visit 3, 4 & 5 (Phone) | Visit 6 (Phone) | Visit 7 (Phone) | Visit 8 (Office/ Virtual Office) | Visit 9 (Office) | Visit 10 & 11 (Phone) | Visit 12, 13 & 14 (Phone) | Visit 15 & 16 (Office/ Virtual Office) | Visit 17 (Office/ Virtual Office) | Visit 18* (Office) | Visit 19 (Office) | Visit 20 (Office **) | Visit 21 (Office **) | Visits 22, 23, etc. (Office **) |
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| hyperglycemia including diabetic ketoacidosis and HHS | | | | | | | | | | | | | | | | |
| Instruct study subjects that regular weekly uploads of the study pump is required. With Bluetooth connection and the MiniMed Clinical 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. | | X | X | X | X | X | X | X | X | X | X | If applicable | X | X | X | X |
| Instruct subjects to give meal bolus of insulin 15-20 minutes before meals during the run-in period and study period | | X | X | X | X | X | | | | | | | | | | |

# 19. Version History

| Version | Summary of changes | Author(s)/Title |
|---|---|---|
| A.1 | • Not Applicable, New Document | [redacted] |
| A.2 | • See "Attachment 1: CIP341 Description of Protocol Changes Version A.1 to A.2" for details on changes<br>• Updated IDE number<br>• Updated glossary<br>• Updated study product to remove/update descriptions, harmonized throughout protocol<br>• Updated study design<br>• Updated sample size and investigational centers<br>• Updated study duration<br>• Updated inclusion/exclusion criteria<br>• Updated study visit schedule and visit schedule figure<br>• Updated study visit details (Table 3)<br>• Added section for "Risks associated with rapid weight loss"<br>• Added section for "Transition of subjects on MDI therapy to/from pump therapy"<br>• Added section "Risk associated with non-insulin anti-diabetic medications"<br>• Updated details regarding recording data<br>• Updated deviation handling<br>• Added section "lost to follow-up"<br>• Updated risk prevention and mitigation (Table 4)<br>• Administrative changes throughout | [redacted] |
| A.3 | • See "Attachment 1: CIP341 Description of Protocol Changes Version A.2 to A.3" for details on changes<br>• Updated glossary<br>• Added section "Risk Associated with SGLT Therapy"<br>• Administrative changes throughout | [redacted] |
| A (Equivalent to FDA Version A.4) | • See "Attachment 1: CIP341 Description of Protocol Changes Version A.3 to A.4" for details on changes<br>• Updated language for sample size<br>• Administrative changes throughout | [redacted] |

| Version | Summary of changes | Author(s)/Title |
|---|---|---|
| B (Equivalent to FDA Version B.1) | • See "Attachment 1: CIP341 Description of Protocol Changes Version A to B.1" for details on changes<br>• Added "tablet" to device listing<br>• Updated "Exclusion Criteria"<br>• Updated "Schedule of Events" section<br>  ○ Updated "Visit Schedule" figures<br>  ○ Updated "Study Visit Schedule & Scheduled Follow-up Visit Windows" section<br>  ○ Updated "Table 3. Study Visit Details"<br>• Administrative changes throughout | [redacted] |
| C.1 | • See "Attachment 1: CIP341 Description of Protocol Changes Version B to C.1" for details on changes<br>• Updated to latest version of CIP Template<br>• Added "Continued Access Period" throughout protocol<br>  ○ Updated "Duration"<br>  ○ Updated "Endpoints"<br>  ○ Updated "Table 3. Study Visit Details"<br>  ○ Updated "Final Reports" section<br>  ○ Updated visit schedule figures<br>• Updated "Inclusion Criteria" to add the use of commercially available biosimilar insulins<br>• Added Visit 16 and updated throughout protocol<br>• Updated "Table 2. Product Accountability Requirements"<br>• Updated "Data Monitoring Committee" section<br>• Administrative changes throughout | [redacted] |
| C.2 | • See "Attachment 1: CIP341 Description of Protocol Changes Version C.1 to C.2" for details on changes<br>• Updated "Inclusion Criteria" to update language to use of Admelog insulin<br>• Updated "Study Design"<br>• Updated "Endpoints"<br>• Updated "Visit Schedule"<br>• Updated "Table 3. Study Visit Details"<br>• Updated "Section 9.9 Study Stopping Rules"<br>• Administrative changes throughout | [redacted] |
| C.3 | • See "Attachment 1: CIP341 Description of Protocol Changes Version C.2 to C.3" for details on changes<br>• Updated "Visit Schedule"<br>• Updated "Table 3. Study Visit Details"<br>• Updated "Section 11.4 Notification of Adverse Events"<br>• Updated "Section 11.5 Expedited Safety Reporting Requirements" | [redacted] |

| Version | Summary of changes | Author(s)/Title |
|---|---|---|
| | • Updated "Section 12 Data Monitoring Committees" section<br>• Administrative changes throughout | |
| C (Equivalent to FDA Version C.4) | • See "Attachment 1: CIP341 Description of Protocol Changes Version B to C" for details on changes<br>• Updated term to "SGLT inhibitor" throughout<br>• Updated "Table 3. Study Visit Details"<br>• Updated "Section 9.8 Subject Exit, Withdrawal or Discontinuation"<br>• Administrative changes throughout | [redacted] |
| D.1 | • See "Attachment 1: CIP341 Description of Protocol Changes Version C.4 to D.1" for details on changes<br>• Transferred CIP to the revised CIP template (Version E)<br>• Added Disposable Sensor 5 (DS5) and MiniMed 780G BLE 2.0 insulin pump to study<br>• Updated to add phases to the study (Phase 1 and Phase 2) and updated sections throughout<br>  ○ Updated "Section 3.1 Background"<br>  ○ Updated "Section 4 Objectives and Endpoints"<br>  ○ Updated "Section 5 Study Design"<br>  ○ Updated "Section 6 Product Description"<br>  ○ Updated "Section 9 Study Procedures"<br>  ○ Updated "Section 14 Statistical Design and Methods"<br>  ○ Reorganized appendices and added "Section 18.4 Appendix 4: Phase 1"<br>• Updated regulatory status of Medtronic Extended Reservoir<br>• Updated exclusion criteria #31 and added exclusion criteria #33<br>• Updated "Section 16.12 Publication and Use of Information"<br>• Updated "Section 18.1.2 Monitor(s) Contact Information"<br>• Updated "Section 18.2 Appendix 2: Labeling of Devices"<br>• Administrative changes throughout | [redacted] |
| D (Equivalent to FDA Version D.2) | • See "Attachment 1: CIP341 Description of Protocol Changes Version C to D" for details on changes<br>• Updated "Section 9.8 Subject Exit, Withdrawal or Discontinuation" | [redacted] |

| Version | Summary of changes | Author(s)/Title |
|---|---|---|
| E.1 (FDA Approved) | • See "Attachment 1: CIP341 Description of Protocol Changes Version D to E.1" for details on changes<br>• Added the MiniMed Mobile App to study and throughout<br>• Updated to specify the completion of Phase 1 and updated relevant sections throughout<br>• Updated number of investigational sites from 30 to 40<br>• Extended total study duration from 30 to 36 months<br>• Added note to Exclusion criteria #15<br>• Updated "Section 3.1 Background"<br>• Updated "Table 3 Visit Details"<br>• Administrative changes throughout | [redacted] |
| E (Equivalent to Version E.2) | • See "Attachment 1: CIP341 Description of Protocol Changes Version D to E (Equivalent to Version E.2)" for details on changes<br>• Added additional model numbers for the Roche Accu-Chek Guide Link Glucose Meter to study and throughout CIP<br>• Updated "Section 18.1.2 Monitor(s) Contact Information"<br>• Updated to latest version of CIP Enterprise Template<br>• Updated copyright year | [redacted] |
| F (Equivalent to FDA Version F.1) | • See "Attachment 1: CIP341 Description of Protocol Changes Version E to F (Equivalent to FDA Version F.1)" for details on changes<br>• Updated sample size | [redacted] |