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Clinical Study Document Approval Form	
Study Name/Identifier	The MiniMed ™ 780G Glycemic Control and Quality of Life Study for the treatment of pediatric and adult subjects with Type 1 Diabetes in France. (EQOL Study) / MDT19028328
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Medtronic Clinical Investigation Plan	
Clinical Investigation Plan/Study Title	The MiniMed™ 780G Glycemic Control and Quality of Life study for the treatment of pediatric and adult subjects with Type 1 Diabetes in France. (EQOL Study)
Clinical Investigation Plan Identifier	MDT19028328
Study Product Name	MiniMed™ 780G System
Sponsor/Local Sponsor	Medtronic France SAS [redacted] The sponsor will maintain a complete list of sponsor staff under a separate cover.
Document Version	Version 4.0 22Oct2020
Lead Principal Investigator	[redacted]

1. Investigator Statement

Study product Name	EQOL
Sponsor	Medtronic France
Clinical Investigation Plan Identifier	MDT19028328
Version Number/Date	Version 4.0 22Oct2020

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

I agree to comply with the latest version of the Declaration of Helsinki, national and local laws, regulations, standards and requirements as specified in section 13.1 of the Clinical Investigation Plan.

I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the evaluation and conduct of the clinical investigation without the prior written consent of Medtronic.

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

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

Table of Contents

2. Glossary

Term	Definition
A1C	Glycosylated or glycated hemoglobin
AE	Adverse Event
CGM	Continuous Glucose Monitoring
CGMS	Continuous Glucose Monitoring System
CIP	Clinical Investigation Plan
CL	Closed Loop
CRF	Case Report Form
CSII	Continuous Subcutaneous Insulin Infusion
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DM	Diabetes Mellitus
DoH	Declaration of Helsinki
DRF	Data Release Form
DTL	Delegated Task List
DTSQ	Diabetes Treatment Satisfaction Questionnaire
DQOL	Diabetes Quality of life
eCRF	Electronic Case Report Form
EC/IRB/HREB/Ethics Board/Head of Medical Institution	Ethics Committee
FDA	Food and Drug Administration
HbA1c	Glycosylated or glycated hemoglobin
HCL	Hybrid Closed Loop
AHCL	Advanced Hybrid Closed Loop

HCP	Health Care Professional
HFS	Hypoglycemia Fear Survey
IC	Informed Consent
IFU	Instructions for Use
LGS	Low Glucose Suspend
MDI	Multiple Daily Injections
OC-RDC	Oracle Clinical Remote Data Capture
PC	Personal Computer
PLGM	Predictive Low-Glucose Management
PRO	Patient-reported outcome
QOL	Quality of Life
RCT	Randomized controlled trial
RF	Radio Frequency
SAP	Sensor Augmented Pump
SG	Sensor Glucose
SMBG	Self-Monitoring of Blood Glucose
TIR	Time in Range
TLS	Transport Layer Security
T1D	Type 1 Diabetes

3. Synopsis

Title	The MiniMed™ 780G Glycemic Control and Quality of Life study for the treatment of pediatric and adult subjects with Type 1 Diabetes in France. (EQOL Study)
Clinical Study Type	Post-Market non-interventional, prospective, local, single-arm, multi-center non-randomized study
Product Name	• MiniMed™ 780G Pump labelled as MiniMed™ Insulin Pump (MMT-1896WWA) - referred to as MiniMed™ 780G Pump throughout the protocol • Guardian™ Link (3) Transmitter Kit (MMT-7910W1) • Guardian™ Sensor (3) Glucose Sensor (MMT-7020D1, MMT-7020C1), referred to as Guardian Sensor (3) throughout this protocol • One-Press Serter (MMT-7512W) -referred to as the Serter throughout the protocol • Accu-Chek® Guide Link Blood Glucose Meter - ROCHE Accu-Chek® (08116083016M)- referred to as the Study Meter throughout this protocol) • MiniMed Reservoir (MMT-332A; MMT-326A) • Infusion sets table list of compatible infusion sets is in table 2. • Activity Guard (ACC-1520) • MiniMed Mobile app (MMT-6101 for Android; MMT-6102 for iOS) • CareLink BLE USB [Blue Adaptor] (ACC-1003911B) • Medtronic CareLink™ Personal for Clinical Research Therapy Management Software (MMT-7338*)* *Note: upload of MiniMed™ system data will be done via Medtronic CareLink™ Personal for Clinical Research Therapy Management Software until the mobile app is available.* Medtronic may incorporate additional/updated devices, software and accessories into this clinical study as they receive appropriate license or regulatory approval and are released commercially by Medtronic.
Sponsor/Local Sponsor	Medtronic France SAS [redacted] *The sponsor will maintain a list of staff under a separate cover*

Indication under investigation	Subjects, 7 years of age and older, with Type 1 Diabetes mellitus (T1D) under Continuous Subcutaneous Insulin Infusion (CSII) therapy ≥6 months with or without Continuous Glucose Monitoring (CGM).
Investigation Purpose	To evaluate the efficacy in glycemic control and the impact on the quality of life of patients using the MiniMed™ 780G System for the treatment of Type 1 diabetes, in real life settings in France.
Product Status	All products have obtained CE mark.
Primary Objective(s)	To evaluate if the MiniMed™ 780G system in Auto Mode increases the proportion of Time In Range (TIR) at 6 months compared to MiniMed™ 780G system in Manual mode (with no SmartGuard™ functions) at baseline. TIR is defined as percentage of sensor glucose values within 70-180mg/dL.
Secondary Objective(s)	Secondary Objective #1: To assess the change of the TIR at baseline and every three months until 12 months. Secondary Objective #2: To evaluate the change from baseline in satisfaction score based on the DTSQc evaluated at 6 months. Secondary Objective #3: To evaluate the change from baseline in quality of life based on the DQoL evaluated at 6 and 12 months. Secondary Objective #4: To evaluate the change from baseline in the fear of hypoglycemic events based on the HFS evaluated at 6 and 12 months. Secondary Objective #5: To evaluate the change of glycemic parameters at baseline and every three months until 12 months and the change in HbA1c from baseline to 6 months and 12 months. Secondary Objective #6: To evaluate the treatment satisfaction score based on the DTSQs evaluated at baseline, 6 and 12 months
Study Design	Local, post-market, non-interventional, prospective, single-arm, multi-center study of patients (Pediatric and adult).
Sample Size	Approximately 300 patients (children and adults) in approximately 32 sites in France.
Duration	It is foreseen that the enrollment period will last for 12 months. The follow up of the patients is of maximum 1-year post Auto Mode activation after baseline visit. Each subject will enter a run-in phase (baseline) in hospital outpatient setting of approximately 2 weeks as per standard clinical practice, followed by a study period of 12 months. Therefore, the maximum duration of subject participation in the study is approximately 12 months. The total study duration is expected to be 2 years.

Inclusion/Exclusion Criteria	Inclusion	Exclusion
	1. Subject is ≥7 years of age. 2. Subject has a clinical diagnosis of type 1 diabetes for more than 1 year as determined via medical records or source documentation by an individual qualified to make a medical diagnosis. 3. Subject has a glycosylated haemoglobin (HbA1c) value greater than 6.5% and less than 12% at time of enrolment visit. 4. Subject is under Continuous Subcutaneous Insulin Infusion (CSII) therapy (with or without Continuous Glucose Monitoring) for 6 months or more before enrolment. 5. Subject requires ≥8 units of insulin per day. 6. Subjects and their parent(s)/guardian(s) must be able to speak and be literate in French as verified by the investigator. 7. Subjects and their parent(s)/guardian(s) are willing to participate in the study and sign the DRF 8. Subjects who are ≥18 years of age should be able to provide consent	1. Subject has MiniMed™ 780G System IFUcontraindication(s). 2. Subject used Predictive Low-Glucose Management (PLGM) System (i.e. MiniMed™ 640G with SmartGuard™) in the last 6 months before the enrolment. 3. Subject used Low Glucose suspend (LGS) feature (i.e. MiniMed™ Paradigm Veo Pump) in the last 6 months before the enrolment. 4. Subject under Multiple Daily Injections (MDI) treatment in the 6 months before the enrolment. 5. Subject has any unresolved adverse skin condition in the area of sensor placement (e.g., psoriasis, dermatitis herpetiformis, rash, hylococcus infection).

Study Procedures and Assessments	Data will be collected as follow: **Baseline** Demographics at Baseline: age, gender. Medical history at Baseline: HbA1c, Previous treatment, Name of the last pump device, Date of the first pump treatment, Number of severe hypoglycemia events in the last year, years since diagnose of T1D; DTSQs; DQoL; HFS. Auto Mode Activation at Baseline: Auto Mode activation date At the end of the run-in period, the following data will be also collected: Mean TIR (70-180mg/dL); Mean Time spent of sensor glucose value below 70mg/dL and below 54mg/dL; Mean Time spent of sensor glucose value above 180mg/dL and above 250mg/dL; Number of bio-chemical hypoglycemic event per week. **6M** DTSQs and DTSQc; DQoL; HFS; Diabetes parameters via CareLink™ Personal for Clinical Research: TIR; Mean time spent of sensor glucose value below 70mg/dL and below 54mg/dL; Mean time spent of sensor glucose value above 180mg/dL and above 250mg/dL; Number of bio-chemical hypoglycemic event per week; HbA1c Number of severe hypoglycemia; Use of Auto Mode; Use of CGM; Number of Auto Mode outings. **12M** DTSQs; DQoL; HFS; Diabetes parameters via CareLink™ Personal for Clinical Research: TIR;

	Mean time spent of sensor glucose value below 70mg/dL and below 54mg/dL; Mean time spent of sensor glucose value above 180mg/dL and above 250mg/dL; Number of bio-chemical hypoglycemic event per week; HbA1c Number of severe hypoglycemia; Use of Auto Mode; Use of CGM; Number of Auto Mode outings. Device data (insulin/CGM) will be collected throughout the study period and evaluated at every 3month.
Safety Assessments	Post-Market surveillance applies only. Adverse Events and Device Deficiencies are not collected. This is an efficacy and Quality of Life and treatment satisfaction non-interventional study. Complaint reporting will be done as per local requirements and Medtronic processes, including vigilance for commercially approved products.
Statistics	The sample size was determined using a one sample paired test assuming a one- sided type I error rate of 0.05 and power greater than 90%. The TIR at baseline is assumed to be around 60% and the TIR at 6 months follow up is assumed to be 63% with standard deviation as 16% and a correlation as 0.5. The sample size needed to demonstrate this hypothesis including 20% of attrition rate is 306. Descriptive statistics will be used to summarize patient characteristics. For categorical variables, the description will consist in frequency and the percentage of each category. For continuous variables, the description will consist summary statistics as mean, standard deviation, standard error, minimum, median and maximum. The primary endpoint on efficacy defined as the change of TIR at 6 months from Auto Mode activation will be analyzed by means of paired (samples) t-test or Wilcoxon signed rank sum test according to the normal or non-normal distribution. The primary outcome will include all patients as the ITT population. Sensitivity analysis will include the per protocol patients as defined by >70% Auto Mode usage.

4. Introduction

4.1. Background

The Medtronic MiniMed™ sensor augmented insulin pumps have been helping insulin requiring patients with diabetes mellitus all around the world for more than two decades. In order to address some of the unmet needs of these patients and to provide them the benefits of newer technologies, Medtronic Diabetes has developed a new Sensor Augmented Pump platform: the MiniMed™ 780G System, also referred as Advanced Hybrid Closed Loop system.

In patients with insulin dependent diabetes mellitus, glycemic control is influenced by numerous factors, such as insulin dosage, insulin absorption, timing, physiological/lifestyle factors such as exercise, food intake, hormones and illness. These factors may contribute to significant variability in insulin requirements, which makes self-management of type 1 diabetes challenging.
Patients who are using continuous glucose monitoring, including sensor-augmented pump therapy, experience improvements in glycemic control. Advanced features of sensor-augmented pump therapy are now being used in clinical practice; these include automatic suspension of insulin delivery when a pre-set glucose threshold is reached (suspend on low) or is predicted to be reached (suspend before low). Both approaches have shown that a significant reduction in the risk and burden of hypoglycemia can be achieved, especially in patients who are prone to experiencing hypoglycemia.
Parallel to these approaches to mitigate the risk of hypoglycemia, more progressive advancements in technology can link insulin delivery directly to glucose levels. Closed-loop insulin delivery is different from conventional pump therapy and low glucose management technology, because it uses a control algorithm to automatically adjust insulin delivery based on subcutaneous sensor data to improve diabetes management. Manual meal-time announcement and prandial insulin boluses still need to be carried out by patients in order to overcome the delay in insulin action of currently available insulin analogues administered subcutaneously. The 'hybrid' closed-loop approach contrasts with a 'fully' closed-loop approach, in which user input to the control algorithm related to meals would no longer be required.

Medtronic has conducted numerous studies to evaluate hybrid closed loop (HCL) technology, currently used in the MiniMed™ 670G System.
The HCL System consists of an insulin pump that delivers insulin to the user, a continuous glucose monitor (CGM) including algorithm that measures the user's glucose levels for up to seven days, and a glucose meter used to calibrate the CGM. The MiniMed™ 670G System is able to decrease or stop insulin delivery when it detects the user's glucose is low or increase the insulin delivery when the system detects the user's glucose levels are high with no input from the user.
After completing a variety of feasibility studies with the hybrid closed loop algorithm, two separate pivotal trials were initiated to show that the use of hybrid closed loop technology (MiniMed™ 670G

System) is safe in both adults and children over the age of 2. In the young adult/adult pivotal study, patients aged 14 to 75 years with type 1 diabetes were recruited from 10 centers (9 in the United States, 1 in Israel). The pediatric pivotal study was conducted as an at-home, multi-center study, which enrolled participants ages 2-13 years. Patients were recruited at 11 centers (10 in the United States, 1 in Israel). The study was identical in design to the young adult/adult pivotal study.
Study results in the pediatric study mirrored data from the pivotal trial of the system in adults and adolescents (14 and above), showing patients spent more time in euglycemic range, experienced less glycemic variability, had less exposure to hypoglycemia and hyperglycemia and significantly reduced HbA1c compared to baseline data, where they used sensor-augmented pumps. No episodes of severe hypoglycemia or diabetic ketoacidosis and no serious device-related adverse events were reported.

The Advanced Hybrid Closed Loop system (AHCL) is based on the MiniMed™ 670G hybrid closed loop system currently in commercial distribution in the United States, Canada and Europe. Relative to the MiniMed™ 670G system, AHCL includes enhancements intended to reduce the frequency of Auto Mode exits and decrease the time spent in hyperglycemia. Advancement such as automatic correction bolusing, sensor glucose based meal bolusing, automatic calibrations of Blood Glucose (BG) measurements transmitted to the pump and a variable target for automatic basal deliveries, all maximize the time spent in hybrid closed-loop operation, in order to further improve glucose control and overall user satisfaction.

Patients using the AHCL system will not be required to confirm sensor glucose using SMBG (Self-Monitoring of Blood Glucose) measurement before making therapy adjustments based on displayed sensor glucose values.
The advanced algorithm receives continuous glucose monitoring (CGM) data every 5 minutes, and a “basal rate” insulin delivery is computed and adjusted every five minutes. Therefore, standard “basal” insulin that is pre-programmed in regular insulin pump therapy is replaced by the algorithm derived insulin delivery (given as a micro-bolus every 5 minutes).
Meals will be announced, and sensor glucose based insulin bolus for a meal will be delivered according to the individualized patient carbohydrate ratio and insulin sensitivity factor.

The MiniMed 780G system is intended for the continuous delivery of basal insulin at selectable rates, and the administration of insulin boluses at selectable amounts. The system is also intended to continuously monitor glucose values in the fluid under the skin. The MiniMed 780G system includes SmartGuard technology, which can be programmed to provide an automatic adjustment of insulin delivery based on continuous glucose monitoring (CGM) and can suspend the delivery of insulin when the SG value falls below, or is predicted to fall below, predefined threshold values.

The MiniMed™ 780G system received CE (Conformité Européenne) Marking in June 2020. While in the United States, the MiniMed™780G system is for investigational use only, and not approved for

sale or distribution.

Several clinical studies were conducted (Table 1) to demonstrate the safety and effectiveness of the MiniMed™ 670G and 780G Systems. However, data regarding the effect on glycemic control, quality of life and treatment satisfaction of MiniMed™ 780G System under the routine practice in France are highly recommended by the French National Authority for Health (HAS).

Table 1: Clinical Program MiniMed™ HCL and AHCL Systems

Study	Sponsor	Design	Population	System	Manuscript
Hybrid Closed Loop Pivotal Trial in Type 1 Diabetes NCT02463097	Medtronic	Pivotal trial (US and Israel)	Age 14-75	HCL	Published by Garg et al. "Glucose Outcomes with the In-Home Use of a Hybrid Closed-Loop Insulin Delivery System in Adolescents and Adults with Type 1 Diabetes" Diabetes Technol Ther. 2017 Mar;19(3):155-163. doi: 10.1089/dia.2016.0421. Epub 2017 Jan 30.
Safety Evaluation of the Hybrid Closed Loop (HCL) System in Pediatric Subjects with Type 1 Diabetes NCT02660827	Medtronic	Interventional, non-randomized, single-arm, multicenter trial (US and Israel)	Age 2-13	HCL	Published by Forlenza et al. "Safety Evaluation of theMiniMed™ 670G System in Children 7-13 Years of Age with Type 1 Diabetes." Diabetes Technol Ther. 2019 Jan;21(1):11-19. doi: 10.1089/dia.2018.0264. Epub 2018 Dec 26.
Multi-center Trial in Adult and Pediatric Patients With Type 1 Diabetes Using Hybrid Closed Loop System and Control at Home NCT02748018	Medtronic	Interventional, randomized controlled trial (RCT) (US, Canada, Europe)	Age 2-80	HCL	Ongoing recruitment

Safety Evaluation of the Advanced Hybrid Closed Loop (AHCL) System in Type 1 Adult and Pediatric Subjects G190075	Medtronic	Interventional, non-randomized, multi-center, single arm (US)	Age 7-75	AHCL	Completed 2020
ADAPT ADvanced Hybrid Closed Loop study in Adult Population with Type 1 Diabetes: A Prospective, Open-label, Multi-center, Adaptive, Confirmatory and Randomized Controlled Study	Medtronic	Pre-market. Prospective, Open-label, Multi-center, Adaptive, Confirmatory and Randomized Controlled Study (EMEA)	Age ≥ 18	AHCL	Ongoing recruitment

4.2. Purpose

Medtronic France SAS is sponsoring the CIP328 EQOL study, a Post-Market non-interventional, prospective, local, single-arm, multi-center non-randomized clinical study. The purpose of this study is to evaluate the impact on glycemic control and quality of life of patients using the MiniMed™ 780G System for the treatment of Type 1 diabetes, in real life settings in France to support reimbursement of the MiniMed™ 780G in France. This data will complete the available data from international pivotal studies, as it is highly recommended by the French authorities to provide local data on glycemic control, quality of life and treatment satisfaction in real life conditions.

5. Objectives and Endpoints

5.1. Primary Objective and Endpoint

The primary objective is to evaluate if the treatment of T1D with MiniMed™ 780G System in pediatric and adult population increases the Time In Range (TIR) at 6 months compared to MiniMed™ 780G System in Manual Mode (with no SmartGuard™ functions) during the run-in period (expected to be approximately 2 weeks). TIR is defined as time spent of sensor glucose values within 70-180mg/dL.

The primary endpoint is the change in (%) the time spent within range (TIR) defined as the proportion of sensor glucose concentration within the target range 70-180 mg/dL (3·9–10·0 mmol/L) between baseline and 6 months.

5.2. Secondary Objectives and Endpoints

Secondary objectives will aim at evaluating the difference in time in range, quality of life and treatment satisfaction.

1) Secondary objective #1: To assess the change of the TIR collected at baseline and every three months until 12 months
2) Secondary Objective #2: To evaluate the change from baseline in satisfaction score based on the DTSQc evaluated at 6 months.
3) Secondary Objective #3: To evaluate the change from baseline in quality of life based on the DQoL evaluated at 6 and 12 months.
4) Secondary Objective #4: To evaluate the change from baseline in the fear of hypoglycemic events based on the HFS evaluated at 6 and 12 months.
5) Secondary Objective #5: To evaluate the change of glycemic parameters at baseline and every three months until 12 months and the change in HbA1c from baseline to 6 months and 12 months.
6) Secondary Objective #6: To evaluate the treatment satisfaction score based on the DTSQs evaluated at baseline, 6 and 12 months

Secondary Endpoints:

a) Secondary endpoint #1: The Time In Range (TIR) defined as the proportion of sensor glucose concentration within the target range of 70-180 mg/dL (3·9–10·0 mmol/L) every 3 months.
b) Secondary Endpoint #2: The different DTSQc versions will be used to assess satisfaction in the following populations:
    a. DTSQc Adult (≥18 years old)
    b. DTSQc Teen (13-17 years old)
    c. DTSQc Parent (7-12 years old)
c) Secondary Endpoint #3: the DQOL questionnaire will be used and the mean scores will be compared between baseline and 6 and 12 months. The different DQOL versions will be used

to assess quality of life in the following populations:

a. DQOL Adult (≥18 years old)
b. DQOL Adult with Adolescent-oriented items (13-17 years old)
c. No DQOL version and therefore collection for patients 7-12 years old

d) Secondary Endpoint #4: the HFS questionnaire will be used and the mean scores will be compared between baseline and 6 and 12 months. The different HFS versions will be used to assess the fear of hypoglycemic events in the following populations:
   a. HFS Adult (≥18 years old)
   b. HFS Teen (13-17 years old)
   c. HFS Parent (7-12 years old)
e) Secondary Endpoint #5: The time of sensor glucose values below 70mg/dL and below 54mg/dL, time of sensor glucose values above 180mg/dL and above 250mg/dL at baseline and every 3 months. The change in HbA1c from baseline to 6 and 12-month follow up.
f) Secondary Endpoint #6: The different DTSQs versions will be used to assess satisfaction in the following populations:
   a. DTSQs Adult (≥18 years old)
   b. DTSQs Teen (13-17 years old)
   c. DTSQs Parent (7-12 years old)

6. Study Design

This study is a local, post-market, non-interventional, prospective, single-arm, multi-center, non-randomized study assessing the glycemic control effect, treatment satisfaction and the quality of life of patients using MiniMed™ 780G System as per the standard care of practice. This study has a single-arm design which will recruit a maximum of 300 subjects in up to 32 sites in France. At the time of Clinical Investigational Plan finalization, the list of participating sites was not finalized. The complete list, which includes the name, position, address and contact details of the investigators responsible for conducting the study for each investigational site, will be available under separate cover and provided to the sites.

To avoid introduction of bias to the study results due to disproportionate enrollment, enrollment at any individual site should not exceed 10% (30 subjects) of the total sample size. It's expected that sites enroll a minimum of 10 subjects per site.
Enrollment will be competitive across study sites. The per-study site enrollment cap may be increased upon Sponsor approval.

Subject enrolled in this study (or his/her parent/legal representative in case of DTSQ and HFS for patients 7-12 years old) will be asked to complete the questionnaires DTSQ, DQoL (if patient is ≥13 years old) and HFS at baseline/enrollment visit and at 6- and 12- month follow-up visits.

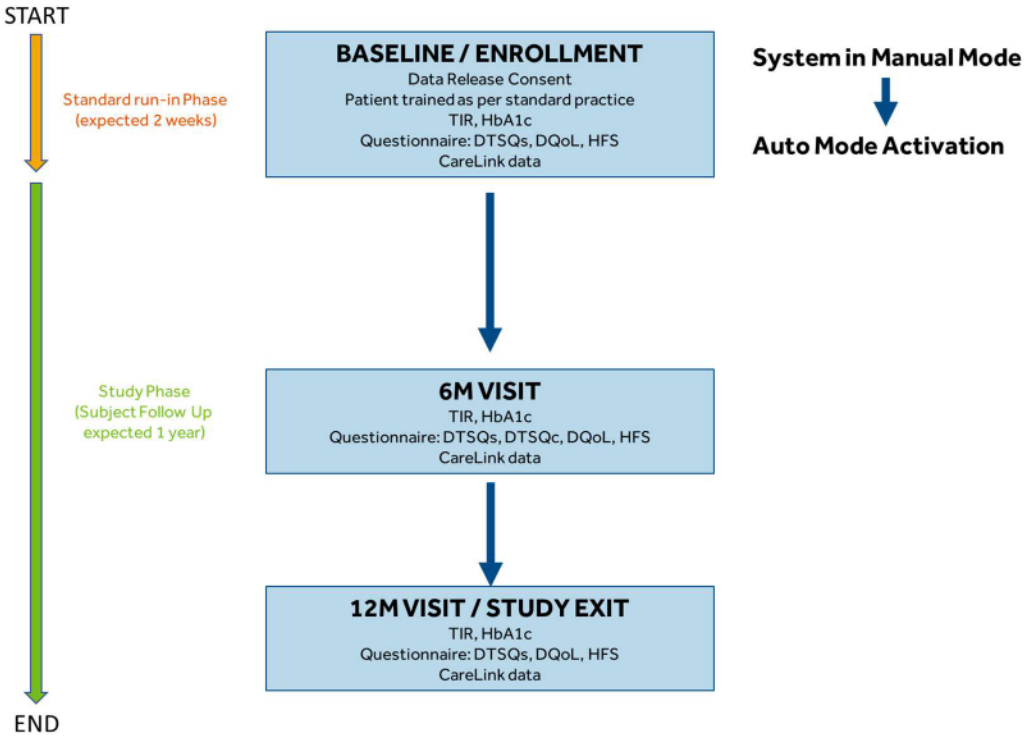
The following measures are taken to minimize potential sources of bias:

- A multi-center design is used to ensure a representative sample of physicians providing the

treatment and to reach a reasonable enrollment period.

- Site selection will be done per predefined selection criteria.
- Only physicians that have adequate documented experience in diabetes management will participate.
- Site training is performed according the training & education plan set up for the pump use in order to assure full understanding and engagement to comply with the pump best utilization.
- Consecutive screening and enrollment will be encouraged and enforced as much as possible.

Figure 1: Study design overview



CareLink™ Personal for Clinical Research data uploads from the devices should be done via Bluetooth connectivity or via USB connection as per clinical practice, i.e. once a week. CareLink™ Data evaluation will be done every 3 months.

Duration

It is foreseen that the enrollment period will last for 12 months. The follow up of the patients i s of maximum 1 year post Auto Mode activation in baseline visit. Each subject will enter a run-in phase in hospital outpatient setting of approximately 2 weeks as per standard clinical practice, followed by a study period of 12 months. Therefore, the maximum duration of subject participation in the study is of approximately 12 months. The estimated study duration is 2 years.

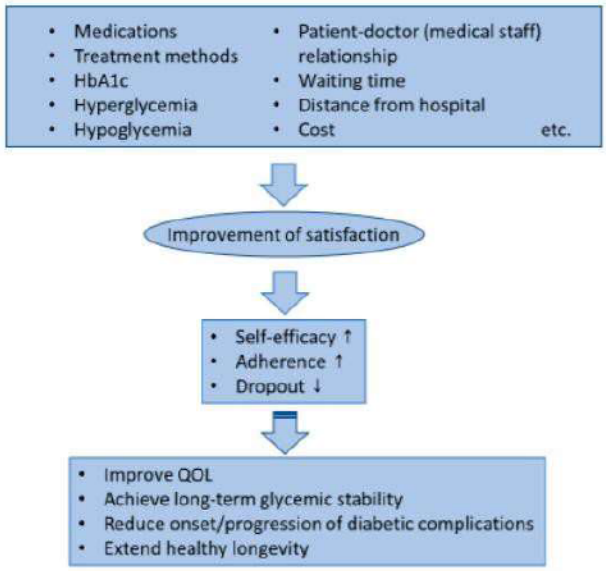
6.1. Rationale

The goal of diabetes treatment is the prevention of the onset and progression of micro- and macrovascular complications as well as the achievement of quality of life (QOL) and longevity equivalent to people without diabetes. Several studies have established the importance of glycemic control to prevent diabetic complications and based on this evidence, a glycated hemoglobin (HbA1c) level of <7% is currently recommended as the glycemic goal in most guidelines [1-4].

However, the outcome of diabetes treatments should not be evaluated only by glycemic control as the evaluation of the psychological aspects of patients, including treatment satisfaction, wellbeing and quality of life (QOL), is also important; they are referred to as patient-reported outcomes (PROs) [5–6].

The improvement in the treatment satisfaction may result in improving patients' self-efficacy and adherence to treatment. The improvement in treatment satisfaction may also reduce the risk of dropout from treatment. Therefore, improvement in treatment satisfaction may foster the achievement of long- term glycemic stability, eventually reducing the risk of developing diabetic complications (Figure 2).

Figure 2: Factors associated with treatment satisfaction and expected effects from its improvement on clinical outcomes



The Diabetes Treatment Satisfaction Questionnaire (DTSQ) is a questionnaire used to assess patients' satisfaction with their diabetes treatment [7]. The questionnaire has been developed to evaluate satisfaction with diabetes treatment regimens in patients with Type 1 and 2 diabetes. There are eight items each rated with a 7-point Likert scale. Six items relate to treatment satisfaction with scores ranging from 0 to 36, higher scores indicating greater satisfaction. Two other items assess perceived frequency of hyperglycemia and hypoglycemia with higher scores reflecting greater problems (Bradley & Lewis 1990). The original 'status' form (DTSQs) focuses on current satisfaction which is reflected in the response options: 6=very satisfied, 0= very dissatisfied. Ceiling effects have been reported and the developers modified the response options to improve precision. This 'change' version (DTSQc) items are equivalent to the DTSQs but response options changed to 3= more satisfied now, -3= less satisfied now with a midpoint of 0 reflecting no change. Responsiveness is reported for both versions but the DTSQc is described as more responsive than DTSQs version [8-9]. DTSQs and DTSQc are recommended by HAS, the French National Authority for Health.

Although the improvement in treatment satisfaction assessed with DTSQ is expected to improve patients' QOL, DTSQ does not assess QOL itself. Indeed, as QOL of patients with diabetes has been shown to be lower, a higher DTSQ score does not necessarily translate into higher QOL [5]. Thus, the use of questionnaires other than DTSQ, such as DQoL, is needed to evaluate QOL. DQoL has been widely used to measure quality of life among diabetes patients [10-11] and contains 46 items used to measure health- related quality of life among diabetes patients based on three main domains, namely, "satisfaction," "impact," and "worry."

The Hypoglycemia Fear Survey (HFS) originally was developed to measure behaviors and worries related to fear of hypoglycemia (FOH) in adults with type 1 diabetes. Both the original HFS (HFS-I) and the revised version (HFS-II) are composed of two subscales, the Behavior (HFS-B) and Worry (HFS-W). HFS-B items describe behaviors in which patients may engage to avoid hypoglycemic episodes and/or their negative consequences (e.g., keeping blood glucose [BG] levels above 150 mg/dL, making sure other people are around, and limiting exercise or physical activity). HFS-W items describe specific concerns that patients may have about their hypoglycemic episodes (e.g., being alone, episodes occurring during sleep, or having an accident). Alternative versions of the HFS have been developed for use with pediatric patients with type 1 diabetes and their parents and will be used in the study (14–16).

Following the objective to assess the new patient's pathway and the benefits of MiniMed™ 780G system in real-life settings, the study design aims to follow routine practice, with before/after comparison of the data to show the benefit of the MiniMed™ 780G system on glycemic parameter, patient treatment satisfaction and quality of life.

Due to the nature of the study, no data monitoring committee is needed.

7. Product Description

7.1. General

The Medtronic MiniMed™ 780G System is intended for continuous delivery of basal insulin (at user selectable rates) and administration of insulin boluses (in user selectable amounts) for the management of Type 1 diabetes mellitus in persons, seven years of age and older, requiring insulin, as well as for the continuous monitoring and trending of glucose levels via a sensor in the interstitial fluid under the skin. MiniMed™ 780G system with SmartGuard™ technology adjusts insulin delivery based on sensor glucose (SG) readings. The glucose sensor measures glucose values in the tissue fluid. The glucose values are wirelessly sent to the insulin pump, and displayed along with glucose trend information, alerts, and alarms on the pump screen. The insulin pump delivers a prescribed dosage of insulin through an infusion set. The insulin pump can automatically adjust the delivery of insulin using a mathematical equation, or algorithm that incorporates information from the CGM. The MiniMed 780G insulin pump operates in Manual mode when the SmartGuard feature is inactive.

With the addition of smart device connectivity, the MiniMed™ 780G system will enable users and their care partners to see real-time glucose data and trends on compatible iOS and Android smartphones via apps via Bluetooth® connectivity.

The MiniMed™ 780G System consists of the following devices:

- MiniMed™ 780G Pump labeled as MiniMed™ Insulin Pump (MMT-1896WWA) - referred to as MiniMed™ 780G Pump throughout the protocol
- Guardian™ Link (3) Transmitter Kit (MMT-7910W1)
- Guardian™ Sensor (3) Glucose Sensor (MMT-7020D1, MMT-7020C1), referred to as Guardian Sensor (3) throughout this protocol
- One-Press Serter (MMT-7512W) -referred to as the Serter throughout the protocol
- Accu-Chek® Guide Link Blood Glucose Meter - ROCHE Accu-Chek® (08116083016M)- referred to as the Study Meter throughout this protocol)
- MiniMed Reservoir (MMT-332A; MMT-326A)
- Infusion sets table list of compatible infusion sets is Table 2.
- Activity Guard (ACC-1520)
- MiniMed Mobile app (MMT-6101 for Android; MMT-6102 for iOS)
- CareLink™ BLE USB [Blue Adaptor] (ACC-1003911B)
- Medtronic CareLink™ Personal for Clinical Research Therapy Management Software (MMT-7338*)*

Note: upload of MiniMed™ system data will be done via Medtronic CareLink™ Personal for Clinical Research Therapy Management Software until Mobile app is available.

Medtronic may incorporate updated devices, software and accessories into this clinical study as they receive appropriate license or regulatory approval and are released commercially by Medtronic. EC will be notified of the integrated updates.
Details on the MiniMed™ 780G System Components and consumable materials used in this study are reported in Table 2. CE marked devices will be used within intended use as described in the approved IFU for which CE mark has been obtained. All materials that will or may be in contact with tissues and/or body fluids are presented in the approved IFU.

System data can be uploaded via Medtronic CareLink™ Personal for Clinical Research software or via Mobile app.

Table 2. MiniMed™780G System Components and consumable materials

Device name	MDT Model number/ part number*	Europe
MiniMed™ 780G Pump	MMT-1896WWA	CE Marked
Accu-Chek® Guide Link Blood Glucose Meter - ROCHE Accu-Chek®	08116083016M	CE Marked
CareLink™ BLE USB [Blue Adaptor]	ACC-1003911B	CE Marked
Guardian™ Link (3) Transmitter Kit	MMT-7910W1	CE Marked
Guardian™ Link (3) Transmitter	MMT-7911	CE Marked
Guardian™ Sensor (3) Glucose Sensor	MMT-7020C1	CE Marked
Guardian™ Sensor (3) Glucose Sensor	MMT-7020D1	CE Marked
One-Press Serter	MMT-7512W	CE Marked
Activity Guard (clip protecteur)	ACC-1520	CE Marked
MiniMed Mobile App Android Patients	MMT-6101	CE Marked
MiniMed Mobile App iOS Patients	MMT-6102	CE Marked
Medtronic CareLink™ Personal for Clinical Research Therapy Management Software	MMT-7338	CE Marked
MiniMed Reservoir 3 ml	MMT-332A	CE Marked
MiniMed Reservoir 1,8ml	MMT-326A	CE Marked
MiniMed™ Mio™ Advance	MMT-242A	CE Marked
MiniMed™ Mio™ Advance	MMT-213A	CE Marked
MiniMed™ Mio™ Advance	MMT-243A	CE Marked
MiniMed™ Mio™ Advance	MMT-244A	CE Marked
Microperfuseur Quick-set™	MMT-397A	CE Marked
Microperfuseur Quick-set™	MMT-399A	CE Marked
Microperfuseur Quick-set™	MMT-394A	CE Marked
Microperfuseur Quick-set™	MMT-396A	CE Marked
Microperfuseur Quick-set™	MMT-398A	CE Marked

Quick-serter™ : dispositif d'insertion pour Quick-set™	MMT-305QS	CE Marked
Microperfuseur SureT ™	MMT-866A	CE Marked
Microperfuseur SureT ™	MMT-876A	CE Marked
Microperfuseur Silhouette™	MMT-378A	CE Marked
Microperfuseur Silhouette™	MMT-381A	CE Marked
Microperfuseur Silhouette™	MMT-382A	CE Marked
Microperfuseur Silhouette™	MMT-377A	CE Marked
Sil-serter™ : dispositif d'insertion pour Silhouette™	MMT-385	CE Marked
Microperfuseur Mio™	MMT-975A	CE Marked
Microperfuseur Mio™	MMT-965A	CE Marked
Microperfuseur Mio™	MMT-943A	CE Marked
Microperfuseur Mio™	MMT-923A	CE Marked
Microperfuseur Mio™30	MMT-905A	CE Marked
Microperfuseur Mio™30	MMT-906A	CE Marked

*MMT numbers may change if other compatible infusion sets become available

7.1.1. MiniMed™ 780G Insulin Pump

The MiniMed™ 780G Insulin Pump (Figure 3) is intended for continuous insulin delivery, at set and variable rates, and administration of insulin boluses, in user selectable amounts, for the management of diabetes mellitus in persons requiring insulin. When used with the CGM components (Guardian™ Sensor (3), Guardian™ Link (3) Transmitter), the pump system is capable of continuous or periodic monitoring of glucose levels in the interstitial fluid under the skin and detection of possible low or high blood glucose episodes. The pump also displays continuous glucose values, storing this data so that it can be retrospectively analyzed to track patterns and improve diabetes management.

The MiniMed™ 780G Insulin Pump also includes the closed loop algorithm as part of the SmartGuard™ collection of features that may be enabled by the user. SmartGuard™ is comprised of Manual Mode Low Management, which includes the suspend on low feature (suspends insulin delivery when a pre-set low Sensor Glucose (SG) threshold is reached), the suspend before low feature (enables insulin to suspend 30 minutes before a pre-set low SG threshold is reached), and Auto Mode (Advanced hybrid closed loop (AHCL)) feature. The Auto Mode and Manual Mode Low Management features will not be active at the same time.

The pump may also be used as a simple pump without CGM or as a sensor augmented pump without the SmartGuard™ features.

The system has two modes: Manual Mode and Auto Mode. In Manual Mode, the system can be programmed by the user to deliver basal insulin at a pre-programmed constant rate. The system can automatically suspend delivery of insulin if the sensor glucose value falls below or is predicted to fall

below a predetermined threshold. The system will then also automatically resume delivery of insulin once sensor glucose values rise above or are predicted to rise above a predetermined threshold. In Auto Mode, the system can automatically adjust basal insulin by continuously increasing, decreasing, or suspending delivery of insulin based on CGM values. Although Auto Mode can automatically adjust basal insulin delivery without input from the user, the user must still manually deliver insulin therapy during meals.

When Auto Mode is enabled on the MiniMed™ 780G insulin pump, the sensor glucose values (SGVs) received from the Guardian™ Link (3) Transmitter by the insulin pump will be used to automatically calculate the basal insulin dose. It will then deliver insulin to the patient, at five-minute intervals, to achieve glycemic control.

With the AHCL system, subjects must still deliver bolus insulin for meals as calculated by the insulin to carbohydrate ratio. This ratio is determined by the Health Care Professional (HCP)/patient. In addition, the setting for active insulin must be programmed at the time Auto Mode is enabled. Basal rates are set for period of open loop therapy, exit from Auto Mode.

When Auto Mode is not enabled, the user may enable the Manual Mode, Smart Guard™ Low Management feature. Here, basal rate delivery will be suspended either when the SGV reached a programmed low threshold (Suspend on Low) or before the SGV has reached the programmed low threshold (Suspend before Low). If the Low Management features were programmed at the time Auto Mode was enabled, they will be automatically available in the event of an exit from Auto Mode.

Compared to the MiniMed 670G system, the AHCL MiniMed 780G system includes the following advanced features:

- Automatic Correction Bolus: Automatic correction boluses that can be based on SG values and a lowered correction target from 150 to 120 mg/dL (8.3 to 6.7 mmol/L) to increase Time in Range (TIR).
- Safe Meal Bolus algorithm: Reduction of the amount of a meal bolus, if it is predicted to increase the risk of post-prandial hypoglycemia to increase TIR.
- SG Based meal bolus: Patients have the option to use a sensor glucose value to bolus for meals
- Auto-Basal Control: Optional lower basal rate target in Auto Mode, either 120mg/dL (6.7 mmol/L) or 110 mg/dL (6.1 mmol/L) or 100 mg/dL (5.6 mmol/L)
- Confirmed Calibrations: Each Blood Glucose Measurement is used as a calibration resulting in less unnecessary Auto Mode exits and missed calibrations, and consequently in less alarms to increase TIR and user satisfaction.

Figure 3. MiniMed™780G Insulin Pump

7.1.2. Guardian™ Sensor (3)

The Guardian™ Sensor (3), referred to as Guardian™ Sensor (3) in this protocol, is a subcutaneous sensor that contains a microelectrode with a thin coating of glucose oxidase beneath several layers of biocompatible membrane. It is intended to penetrate the skin at a 90-degree angle and is shorter and thinner than the previous generation of MiniMed™ sensors. An introducer needle penetrates the skin surface and provides support for the sensor microelectrode during insertion. The electrode tubing maintains the electrode structure by providing support during and after subcutaneous 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.

Figure 4: Guardian™ Sensor 3

7.1.3. One-Press Serter

The One-Press Serter, referred to as the Serter (Figure 5) in this protocol, is an insertion device that is used to ensure correct placement of the Guardian™ Sensor (3) into the user's subcutaneous tissue. Insertion is triggered when the two spring loaded buttons on the sides of the Serter are pressed simultaneously. The Serter is intended as a non-sterile and multi-use device. It is indicated for single-patient use and is not intended for multiple patient use.

Figure 5. One-Press Serter

7.1.4. Guardian™ Link (3) Transmitter

The Guardian™ Link (3) transmitter with Bluetooth™* wireless technology is a rechargeable device and powers the glucose sensor, collects and calculates the sensor data, and sends the data to a compatible MiniMed™ insulin pump system with smart device connectivity for the management of diabetes mellitus.

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

In addition, the transmitter also contains the sensor calibration algorithm which converts the sensor signal to a SG value using calibration blood glucose (BG) values from a meter relayed to the transmitter through the pump. The transmitter transmits the calculated glucose data to the pump via 2.4GHz RF technology (Tel-D communication protocol) and Bluetooth™ wireless technology. The new algorithm is designed to improve and optimize performance when paired with the Guardian™ Sensor (3). Some elements of the new calibration logic include prompting the user to calibrate when needed, referred to as “Smart Cal,” instead of strictly scheduled time-based calibration requirements.

The transmitter is attached to the sensor via a connector and a tape is applied on top of the sensor.

Figure 6: Guardian™ Link (3) Transmitter

Transmitter

Transmitter + Sensor

7.1.5. Transmitter Charger

The Transmitter Charger (Figure 7) is used to recharge the Guardian™ Link (3) Transmitter as needed. The transmitter contains a non-replaceable, rechargeable battery. A fully charged battery provides up to 7 days of Guardian™ Link (3) Transmitter use. The system includes a battery charger that will recharge the device according to the user guide.

Figure 7. Transmitter Charger

7.1.6. Tester

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

7.1.7. Accu-Chek® Guide Link Blood Glucose Meter - ROCHE Accu-Chek®

Accu-Chek® Guide Link Blood Glucose Meter by Roche, referred to as the Study Meter throughout protocol, will be provided to study participants for use with the MiniMed™ 780G Insulin Pump. The meter measures a subject's capillary blood glucose level using the Accu-Chek® Guide Linkby Roche, which is then used to calibrate the pump.

Accu-Chek® Guide Link meter Blood Glucose Monitoring System sends BG meter readings directly to the pump. When an Accu-Chek® Guide Link meter is used, the reading appears on the Home screen when the Sensor feature is off. The MiniMed 780G insulin pump with smart device connectivity can pair only with an Accu-Chek® Guide Link meter to automatically receive BG readings. If the Accu-Chek® Guide Link meter is not paired with the pump, enter BG readings manually.
Accu-Chek® Guide Link with the newest Bluetooth Low Energy (BLE) technology. The BLE allows for low-energy connectivity to the associated Accu-Chek® Connect diabetes management app.

The MiniMed™780G Insulin Pump uses the calibration point in the real- time algorithm which calculates the SGVs that are displayed to the subject. The result of the finger stick (capillary Self-Monitoring of Blood Glucose (SMBG)) reading performed is entered into the AHCL MiniMed™780G Insulin Pump and can be stored in its memory as a glucose point. The MiniMed™780G Insulin Pump

asks the user every time a calibration is needed, if the user wants to use the linked meter Blood Glucose for calibration. If yes is selected, the glucose value will be stored in memory as a calibration point.

Figure 8: Accu-Chek® Guide Link Blood Glucose Meter - ROCHE Accu-Chek®

7.1.8. Medtronic CareLink™ Personal for Clinical Research Therapy Management Software for Diabetes

Medtronic CareLink™ Personal Therapy Management Software for Diabetes is a web-based system that allows the device data to be viewed and easily evaluated by the physician. A personal computer (PC) links to the Medtronic CareLink™ Personal system via the Internet and allows for upload of data from MiniMed™ insulin pump and third-party blood glucose meters. For the purposes of this study, uploads are performed both by the Investigational Center staff and subjects.

The data contained in CareLink™ Personal is accessible to users using a standard browser, e.g., Microsoft® Internet Explorer on an Internet enabled PC and a unique username (XXX-XXX-XXX) and password created for each patient, per standard of care.

The system uses standard Transport Layer Security (TLS) technology. TSL 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:

1. The internet to the web server;
2. Web server to the application server;
3. Application server to the database server.

7.1.9. Other supplies Infusion sets, Reservoirs and Infusion Set Serter Devices

All consumables for pump therapy will be provided, including:

7.1.9.1. Infusion Sets

Available infusion sets are the following:

- Quick Set Infusion sets
- Silhouette Infusion sets
- Sure-T Infusion sets
- Mio Infusion sets
- Mio 30 Infusion sets
- Mio Advance Infusion sets

Note: Medtronic may incorporate additional infusion sets into this clinical study as they become commercially available. Instructions for the infusion sets used in this study are provided in their respective manuals. All infusion sets provided to subjects must be approved for use with MiniMed™ 780G for rapid- acting analogue insulin Humalog, Novorapid and Novolog.

7.1.9.2. Infusion Set Serter Devices

Available infusion set serter devices are:

- Quick-Serter
- Sil-Serter

The devices are indicated for single patient multi use, i.e. a patient uses the same serter every 2 to 3 days to insert a new infusion set as described in the IFU. All infusion set serter devices provided to subjects must be approved for use with MiniMed™ 780G System for rapid-acting analogue insulin Humalog, Novorapid and Novolog.

7.1.9.3. Reservoirs

Patients are instructed to change their reservoir every 2 to 3 days. All reservoirs provided to subjects must be approved for use with MiniMed™ 780G System for rapid-acting analogue insulin Humalog, Novorapid and Novolog. The reservoir stores insulin for delivery and is inserted into the pump reservoir compartment.

7.1.10. MiniMed Mobile App Patients

The Mobile app provides a secondary display of insulin pump data and CGM, and uploads system data to CareLink™ software. The glucose levels can be viewed on the smartphone, allowing an easily glucose trend monitoring, and the Mobile app provides notifications if there are high or low blood glucose level. It is available to download at no cost for most iOS and Android smartphones.

7.1.11. CareLink™ BLE USB [Blue Adaptor]

Blue Adapter uploads system data from the MiniMed 780G pump to the CareLink™ software through a USB port on a computer.

Figure 9: CareLink™ BLE USB [Blue Adaptor]

7.2. Manufacturer

Except for the Accu-Chek® Guide Link Blood Glucose Meter - that is produced and distributed by ROCHE, all other components of the MiniMed™ 780G System are produced and distributed by Medtronic.
The manufacturer is listed below:

- Medtronic MiniMed™ 18000 Devonshire Street
- Northridge CA, 91325 USA
- Unomedical a/sAaholmvej 1-3, Osted4320 Lejre Denmark

7.3. Packaging

All devices will be labelled in accordance with local language requirements.

Study pump, study meters and sensors are supplied with additional commercially available materials (i.e., alcohol wipes, tape, etc.) free of charge.

7.4. Intended Population

The study will be proposed to patients with type 1 diabetes mellitus. The intended population must comply with the therapeutic indication of the MiniMed™ 780G System as described in the approved IFU for which CE mark has been obtained.

7.5. Product Use

Devices should be used within the intended use described in the approved IFU for which CE mark has been obtained for subjects who meet the eligibility criteria for the study.

There will be no specific procedure within this study for the management of MiniMed™ 780G System since it is a non-interventional study conducted according to routine practice and on CE marked devices. Additional device traceability is not applicable for this registry. There will be no device log in the Investigator Site File.

7.6. Product Training Materials

Training of the center staff on the conduct of the study will be initiated before the protocol is implemented. All participating physicians and other stakeholders will be familiarized with the system as per standard practice. Training contains both lecture and hands-on experience.

People in charge to follow the subjects may be present for the training and study follow-up visits to provide technical support.

7.7. Product Storage

It is the responsibility of the investigator to correctly handle and store market released product. These products will be used according to their labeling.

7.8. Product Accountability

All products used in this study will be market released in the geographies they are used. Device Traceability may be required per local laws and regulations. If there are additional local requirements related to the system beyond what is collected by Medtronic on the eCRF, this is the Investigator's responsibility and should be recorded in the subject's medical records, but will not be collected by Medtronic (e.g., national registration card number, identification code linked to names and contact information, log of all subjects enrolled in the study, lot or batch number).

8. Study Site Requirements

8.1. Investigator/Investigation Site Selection

All investigators managing the subject must be qualified practitioners and experienced in the diagnosis and treatment of subjects with Type 1 Diabetes. All physicians must be experienced and/or trained in the handling of MiniMed 780G system.

The role of the principal investigator is to implement and manage the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical investigation.

The principal investigator shall:

- Be qualified by education, training, and experience to assume responsibility for the proper conduct of the clinical investigation
- Be experienced in the field of application and training in the use of MIniMed 780G system
- Investigator is not debarred, disqualified, or working under sanctions in applicable regions
- Be able to demonstrate that the proposed investigational study site:
  - Has the required number of eligible subjects needed within the recruitment period
  - Has one or more qualified investigators, a qualified investigational study site team and adequate facilities for the foreseen duration of the clinical investigation

Study site personnel training will be completed and documented prior to participation in this study.

An investigator/investigation site may be included in the investigation if the investigator/investigation site complies with the following requirements:

- Site is using Medtronic MiniMed™ Pumps as part of their standard of care.
- Site has sufficient resources to conduct the study

8.2. Study Site Activation

During the activation process (prior to subject enrollment), Medtronic will train study site personnel on the clinical investigation plan, informed consent, and on data collection and reporting tools. If new members join the study site team, they will receive training on the applicable study requirements relevant to their role before contributing to the study.

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

- EC approval (and voting list, as required by local law) of the current version of the CIP and IC.
- Fully executed CTA. Medtronic contracts with participating institutions/investigators through a Clinical Trial Agreement that defines the scope and responsibilities and associated compensation related to carrying out the obligations under a clinical study sponsored by Medtronic. A Clinical Investigation Agreement shall be entered into by the participating investigation site and/or the

principal clinical investigator at each investigation site as per the local legal requirements and returned to Medtronic prior to the commencement of any study activities. Whenever possible, the investigator is indicating approval of the Clinical Investigation Plan and subsequent amendments, by signing and dating the agreement.

- Current CV of investigators of the investigation study site team (as required), . A recent signed and dated Curriculum Vitae should be collected from each principal investigator and co- investigators participating in this study, evidencing the required qualifications per local law, including the year and, possibly, where obtained, and shall include their current position at the investigation site.
- Documentation of delegated tasks
- Documentation of study training.
- Additional requirements imposed by local regulations and EC shall be followed, if appropriate.

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

Medtronic will provide each study site with documentation of study site/investigator readiness; this letter must be received prior to performing study related activities.

9. Selection of Subjects

9.1. Study Population

Subjects 7 years of age or older with T1D and under Continuous Subcutaneous Insulin Infusion (CSII) therapy (with or without CGM) may be considered for this study if they meet all of the inclusion and none of the exclusion criteria outlined in this clinical investigation plan.

9.2. Subject Enrollment

The point of enrollment is defined as the time at which the in- and exclusion criteria have been checked and fulfilled and at which the subject (or his/her parent/legal representative) and the principal investigator or authorized designee, as required, have personally signed and dated the Data Release Form (DRF). At that point, the subject is considered enrolled in the study. A study subjects ID number will be assigned, and the subject must be followed until study closure or study exit, whichever occurs first. The investigator will record on the medical file of the subject that he/she participates in this study.

9.3. Inclusion Criteria

- Subject is ≥7 years of age.
- Subject has a clinical diagnosis of type 1 diabetes for more than 1 year as determined via medical records or source documentation by an individual qualified to make a medical diagnosis.
- Subject has a glycosylated haemoglobin (HbA1c) value greater than 6.5% and less than 12% at time of enrolment visit.
- Subject is under Continuous Subcutaneous Insulin Infusion (CSII) therapy (with or without Continuous Glucose Monitoring) for 6 months or more before enrolment.
- Subject requires ≥8 units of insulin per day.
- Subjects and their parent(s)/guardian(s) must be able to speak and be literate in French as verified by the investigator.
- Subjects and their parent(s)/guardian(s) are willing to participate in the study and sign the DRF.
- Subjects who are ≥18 years of age should be able to provide consent.

9.4. Exclusion Criteria

- Subject has MiniMed™ 780G System IFU contraindication(s).
- Subject used Predictive Low-Glucose Management (PLGM) System (i.e. MiniMed™ 640G with SmartGuard) in the 6 months before the enrolment.
- Subject used Low Glucose suspend (LGS) feature (i.e. MiniMed™ Paradigm Veo Pump) in the 6 months before the enrolment.
- Subject under Multiple-Daily Injections (MDI) treatment in the 6 months before the enrolment.
- Subject has any unresolved adverse skin condition in the area of sensor placement (e.g., psoriasis, dermatitis herpetiformis, rash, Staphylococcus infection).

10. Study Procedures

10.1. Schedule of Events

The study is conducted according to the same schedule as the routine follow-up of patients. Every attempt to minimize missed follow-ups should be made.

The study does not require any specific exam or procedure that falls outside routine practice.
An overview of data collection is given in Table 3 below.

Table 3: Schedule of Assessments

Data collection	Enrollment /Baseline	6-month Follow-up (±45 days)	12-month Follow-up (±45 days)
Data Release Form	√		
Inclusion and exclusion criteria	√		
Demographics	√		
Medical history	√		
HbA1c[1]	√	√	√
Auto Mode Activation Date	√		
Ensure that CareLink™ Personal upload was done[2]	√[4]	√	√
CGM data	√	√	√
Study Exit			√
Study Deviation	Upon occurrence		
QUESTIONNAIRES :			
DTSQs	√	√	√
DTSQc		√	
DQoL[3]	√	√	√
HFS	√	√	√

1. Available HbA1c value collected up to 30 days before enrollment and more or less 30 days from 6-month and 12-month follow up visits can be used.
2. CareLink™ data should be uploaded via Bluetooth connectivity from the devices or via USB connection as per clinical practice, i.e. once a week. CareLink™ Data evaluation will be done every 3 months for secondary objectives.
3. DQoL will not be administered in case patient is between 7 and 12 years old.
4. Baseline CGM data will be collected before Auto Mode activation at the end of the run-in phase

Data Release Form will be obtained prior to subject enrollment and/or before any study-specific procedures are initiated. The principal investigator or his/her authorized designee will conduct the Data Release Form process in accordance with local law and regulations.

10.2. Data Collection

Data collection requirements are summarized in Table 4 below.

Table 4: Data collection and study procedure requirements at subject visits. Minimum number of CRF planned at each visit per subject

		Baseline	6M FU	12M FU	Exit	Deviation	Unplanned
CRF Long Name	**eCRF**						
Data Release and Eligibility	**A_CONSENT**	1					
Baseline	**A_Base**	2					
Follow Up	**A_FU**		1	1			
DTSQs Parent	**A_DTSQsP**	3	2	2			
DTSQs Teen	**A_DTSQsT**	4	3	3			
DTSQs Adult	**A_DTSQsA**	5	4	4			
DTSQ change Parent	**A_DTSQcP**		5				
DTSQ change Teen	**A_DTSQcT**		6				
DTSQ change Adult	**A_DTSQcA**		7				
DQOL	**A_DQOL**	6	8	5			
HFS Parent	**A_HFS_P**	7	9	6			
HFS Teen	**A_HFS_T**	8	10	7			
HFS Adult	**A_HFS_A**	9	11	8			
Auto Mode Activation	**A_AUTOMOD**	10					
Study Exit	**A_EXIT**				1		
Protocol Deviation	**A_PROT_DEV**					1	x

10.3. Enrollment/baseline visit

The investigational center will not initiate any subject activities until EC approval (and all necessary approvals) has been granted. The investigator will check the study eligibility based on a patient meeting, all the study inclusion criteria and none of the exclusion criteria. Investigator will inform the patient about the study and will provide him/her the EC approved Data Release Form. After subjects having given their written Date Release consent, they are considered enrolled in the study and the following information will be collected:

Baseline:

- Demographics
  - Age, sex
- Medical history
  - HBA1c (available value collected up to 30 days before enrollment can be used)
  - Previous treatment
  - Name of the last pump device

- Date of the first pump treatment
- Years since diagnose of T1D
- Number of severe hypoglycemia in the last year

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

- Questionnaires
  - DTSQs
  - DQoL (except for patients between 7 and 12 years old)
  - HFS

The questionnaires will be completed following the specific, standardized instructions in the waiting room and returned the same day. Paper versions of the questionnaires will be made available for this purpose.

To minimize any bias, subjects will fill out the questionnaire before they get equipped by the MiniMed™ 780G insulin pump, before clinician assessments and discussion of their clinical condition, and any other related topics that could influence patient's perception and feelings prior to responding to the questions.

Once eligibility has been confirmed, subject will start a run-in phase in a hospital outpatient setting, as per standard practice of the site.

The objective of the run-in phase is to train the subjects on the MiniMed™ 780G insulin pump, assess subjects' compliance and ability to comprehend the study procedures and tolerance of wearing the sensor and transmitter continuously. It is expected that during the run-in phase the MiniMed™ 780G insulin pump will be set in Manual mode and all the algorithms are switched off, and baseline CGM data will be collected. Data from the MiniMed™ 780G insulin pump will be uploaded in the CareLink™ Personnel for Clinical Research as per standard practice before Auto Mode activation.

Baseline CGM data are listed below:

- Mean TIR (70-180mg/dL)
- Mean Time spent of sensor glucose value below 70mg/dL and below 54mg/dL
- Mean Time spent of sensor glucose value above 180mg/dL and above 250mg/dL
- Number of bio-chemical hypoglycemic event per week

Bio-chemical hypoglycemic events are defined as events with sensor glucose values lower than 54 mg/dL for more than 15 min consecutively.

The expected duration of the run-in phase is approximately 2 weeks. At the end of the run-in phase the MiniMed™ 780G insulin pump will be set in Auto Mode and the date of activation will be collected. and identified as a start of the study phase.

10.4. 6- and 12-month Follow-up Visits

Subsequent follow-up visits will be performed according to the therapy management standard of care at 6 and 12 months after Auto Mode activation in the study.

During the follow-up visits, patients will be asked to fill-out the following questionnaires:

Table 4: Questionnaires to be completed

	6 Month FU	12 Month FU
DTSQs	√	√
DTSQc	√	
DQoL	√	√
HFS	√	√

All questionnaires have been designed for self-completion. When available (e.g. DTSQ and HFS), specific version of the questionnaires will be completed by a parent for subjects younger than 13 years old. DQOL will not be administered in case patient is between 7 and 12 years old. Patient questionnaires are in a paper form and should be completed on site during routine follow-up visits. It is recommended to administer the DTSQs before the DTSQc.

Patients are followed per standard of care, therefore there are no mandatory visit windows defined in this study, however the visit windows defined below are provided as recommendation and guidance.

- 6 Month FU: Follow-up Office Visit - 180 Days (± 45 days)
- 12 Month FU: Follow up Office Visit - 365 Days (± 45 days)

Data from the MiniMed™ 780G insulin pump will be uploaded in the CareLink™ Clinical for Research as per standard practice. The following data from the CareLink™ will be used to correlate with the QOL data:

- Mean TIR (70-180mg/dL)
- Mean Time spent of sensor glucose value below 70mg/dL and below 54mg/dL
- Mean Time spent of sensor glucose value above 180mg/dL and above 250mg/dL
- Number of bio-chemical hypoglycemic event per week
- Number of severe hypoglycemia,
- Time in Auto Mode,
- Time in CGM,
- Number of Auto Mode outings.

Additionally, the following information will be collected at each visit:

- HbA1c (available value collected ± 30 days from 6-month and 12-month follow up visits can be used).

10.5. Study Exit

A study exit form will be completed for all included subjects. Per normal study completion, the date of the last follow up visit, the 12-month Follow-up visit, will correspond to the study exit date. At the end of the study, the subjects will continue to be treated following the routine practice of each center and physician's discretion.

10.6. Source Data

The investigator will indicate in the clinical records that the subject is enrolled in this clinical investigation.

Subject's medical records, CareLink™ Personal For Clinical Research software data, and questionnaires will be used as source documents. Worksheets can be used as source documentation. The investigator must ensure accuracy, completeness and timeliness of the data reported in the eCRFs. The data in the eCRF should be consistent with the source documentation (including subject medical records, questionnaires and worksheets). Sponsor study personnel will review all eCRFs and create data queries for missing data that impacts data analysis.

The investigator(s) and study personnel must be accessible to the Medtronic clinical study team or any person mandated by Medtronic. This accessibility is of particular importance for the completion and clarification of the data on the eCRF. Access to the subject records and other source data must be provided to study monitors, auditors and/or inspectors. All persons involved within this study are working under medical or professional secret policy.

Where copies of the original source document as well as printouts of original electronic source documents are retained, these shall be signed and dated by a member of the investigation site team.

10.7. Data Release consent process

In advance of the consent discussion, the subject (and his/her parent/legal representative) should receive the Ethic Committee (EC) approved Data Release Form. During the consent discussion, the investigator or his/her authorized designee must fully inform the subject (and his/her parent/legal representative) of all aspects of the clinical study that are relevant to the subject's (and his/her parent/legal representative) decision to participate in the clinical study. All items addressed in the Data Release Form must be explained. The language used shall be native and as non-technical as possible and must be understandable to the subject (and his/her parent/legal representative).

The subject (and his/her parent/legal representative) must have ample time and opportunity to read and understand the Data Release Form, to inquire about details of the clinical study, and to decide whether or not to participate in the clinical study. All questions about the clinical study should be

answered to the satisfaction of the subject (and his/her parent/legal representative). Neither the investigator, nor the investigation site staff shall coerce or unduly influence a patient to participate or to continue to participate in the clinical study. The Data Release Form process shall not waive or appear to waive the patient's subject's rights.

When the subject (and his/her parent/legal representative) decides to participate in the clinical study, the Data Release Form must be signed and personally dated by the subject or parent/legal representative and investigator or authorized designees. Subjects who are 7-17 years old are not required to sign a DRF, their parent/legal representative will sign a DRF on their behalf.

After all persons have signed and dated the Data Release Form, the investigator must provide the subject or parent/ legal representative with a copy of the dated Data Release Form. The original Data Release Form will be kept on-site as part of Investigator Site File (ISF) and the Investigator must document the Data Release Consent process.

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 designees should inform the subject (or his/her parent/legal representative) in a timely manner.

Medtronic will revise the written Data Release Form whenever new information becomes available that may be relevant to the subject's confirmed participation in the clinical study. After approval by the EC, a copy of this information must be provided to the participating subjects (or his/her parent/legal representative), and the Data Release Form process as described above needs to be repeated if the new information is relevant to the subject (and his/her parent/legal representative).

A copy of the Data Release Form will be provided under a separate cover.

10.8. Assessment of Safety

This is a non-interventional study assessing the glycemic control and Quality of Life of subjects with T1D. No Adverse Events or Device Deficiencies are collected, and there are no specific safety parameters to be assessed as part of the study. Complaint reporting will be done as per local requirements and Medtronic processes, including vigilance reporting for commercially approved products.

10.9. Recording Data

This study will utilize a Clinical Remote Data Capture (RDC) system that is the property of Medtronic. Each enrolled subject will be assigned a unique study ID number, which is pre-configured in the RDC system. Records of the subject/subject ID relationship will be maintained by the study site. Individual subject medical information obtained for this study will be considered confidential. The subject's

medical charts must be clearly marked to indicate that subjects are enrolled into the study, per the site's SOPs.

Required data will be recorded on electronic Case Report Forms (CRFs) by authorized site personnel as indicated on the Delegated Task List (DTL), which can be found in the Investigator Site File (ISF). Study personnel delegated for CRF completion will be trained on the use of the RDC system and thereafter provided with a username and password to access the system. The CRFs must be completed and/or updated to reflect the latest observations on the subjects participating in the study. The investigator (or delegated co-investigator) will electronically sign the appropriate pages of each CRF.

The RDC system maintains an audit trail of entries, changes, and corrections in CRFs. If a person only authorized to complete CRFs makes changes to an already signed CRF, the investigator shall re-approve that CRF.

The investigator must ensure accuracy, completeness, legibility and timeliness of the data reported in the CRFs and in all other required reports. Data reported on the CRFs which are derived from source documents must be consistent with the source documents or the discrepancies need to be justified in a documented rationale, signed and dated by an Investigator and filed in the subject's research records at the site.

10.10. Deviation Handling

A CIP and/or study deviation is an event where the investigator or site personnel did not conduct the clinical study according to the Clinical Investigational Plan or Clinical Investigation Agreement.

Example of deviations may include but are not limited to:

- Failure to obtain Data Release Form prior to participation in the study;
- Incorrect version of Data Release form provided to subject;
- Failure to obtain EC approval before the start of the study;
- Subject did not meet enrollment criteria and was enrolled;
- Subject failure to attend a follow-up visit;
- Required assessment/data collection during visit not done;
- Source data permanently lost.

Investigators may not deviate from the CIP, unless the deviation is necessary to protect the rights, safety and wellbeing of the subject in an emergency situation. Deviations should be reported to Medtronic regardless of whether medically justifiable, pre-approved by Medtronic, or taken to protect the subject in emergency. Study deviations should be reported to Medtronic via the study

deviation CRF in a timely manner.

Investigators are also required to adhere to local EC requirements and procedures for reporting study deviations. Reporting of all other study deviations should comply with EC policies and/or local laws and must be reported to Medtronic as soon as possible upon the study site becoming aware of the deviation.

Medtronic is responsible for analyzing deviations, assessing their significance, and identifying any corrective and/or preventive actions that may be warranted. Repetitive or serious investigator compliance issues may represent a need to initiate a corrective action plan, which may include suspension of enrollment or termination of the investigator or site participation in the study.

10.11. Subject Withdrawal or Discontinuation

Participation in this study is voluntary and the study subject has the right to discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. A withdrawn subject will be treated according to standard of medical care and will not be replaced. Subjects will be included in the analyses up to the time that consent was withdrawn.

Subjects may also be withdrawn from the study at the discretion of the Investigator if the patient's well- being is jeopardized by continuation of the study.

If a subject chooses to end his or her study participation or if a subject is removed from the study at the Investigator's discretion, the date, circumstances and the reason for termination must be documented both in source documents and on the appropriate eCRF. No data obtained after withdrawal of consent will be recorded on eCRF.

The study site will make every effort to have all subjects complete the follow-up visit schedule. A subject will not be considered lost to follow-up unless all efforts to obtain compliance are unsuccessful. At a minimum, the effort to obtain follow-up information must include 3 attempts to make contact via telephone and if contact via phone is not successful, a traceable letter from the investigator should be sent to the subject's last known address, a copy of which should be maintained in the subject's study record. If both telephone and mail contact efforts are unsuccessful, the subject's personal physician (if subject confirmed agreement in consent) should be contacted to verify the subject's safety information and vital status (alive or deceased). Subject will then be deemed lost to follow up. All contact efforts to obtain follow-up must be documented in the subject's medical records.

If a subject discontinues the study at any time or is withdrawn from the study early, they should continue to be followed as per standard care.

11. Risks and Benefits

11.1. Potential Risks

The study aims to evaluate the effect on glycemic control, treatment satisfaction and the impact on the quality of life of patients using the MiniMed™ 780G System following the standard care in France. There are no expected additional risks relative to participation in this study as devices used are commercially available and used in accordance with approved labelling.

Furthermore, the study is non-interventional, subjects are treated according to standard clinical practice, therefore there are no additional risks associated with study participation.

Potential risks associated with the use of MiniMed™ 780G System include, but are not limited to the following list:

- Hypoglycemia
- Hyperglycemia
- Diabetic Ketoacidosis
- Seizure
- Coma
- Death

General risks related to insulin pump infusion set may include:

- Localized infection
- Skin irritation or redness
- Bruising
- Discomfort or pain
- Bleeding
- Irritation
- Rash
- Occlusions that can interrupt insulin delivery and lead to hyperglycemia or Diabetic Ketoacidosis

General risks related to sensor use may include:

- Skin irritation or other reactions
- Bruising
- Discomfort
- Redness
- Bleeding
- Pain
- Rash

- Infection
- Raised bump
- Appearance of a small "freckle-like" dot where needle was inserted
- Allergic reaction
- Fainting secondary to anxiety or fear of needle insertion
- Soreness or tenderness
- Swelling at insertion site
- Sensor fracture, breakage or damage
- Minimal blood splatter associated with sensor needle removal
- Residual redness associated with adhesive, tape, or both
- Scarring

Specific risks related to sensor use:

Use of medications with paracetamol, including, but not limited to fever reducers or cold medicine, while wearing the sensor may falsely raise sensor glucose readings and result in an over-delivery of insulin. The level of inaccuracy depends on the amount of paracetamol active in the body and may be different for each person.

Risks related to meter use:

- See the user guide that came with the device for the most current risks.

General risks related to serter use may include:

- The serter contains small parts and may pose a choking hazard that can result in serious injury or death.
- Side effects include discomfort and skin irritation at the insertion site.

11.2. Risk Minimization

The potential risks associated with the MIniMed 780G system were identified and have been successfully mitigated and are addressed in the user guide. There are no expected additional risks relative to participation in this study as devices used are commercially available and used in accordance with approved labelling. Any potential risks associated with this study are further minimized by selecting qualified investigators and training study personnel on the CIP.

Specific risks minimizations related to sensor use include, but are not limited to:

- Use of medications with paracetamol: if paracetamol is taken, stop the use of the medication before using SG readings to make treatment decisions. Use additional BG meter readings to verify glucose levels, turn off the Auto correction feature, and consider turning off the SmartGuard feature. Check the label of any medication to confirm whether paracetamol is an active ingredient.
- Do not use SG values to make therapy treatment decisions while the pump is in Manual

mode. SG values can only be used to make therapy treatment decisions while the SmartGuard feature is active. SG and BG values may differ. If the SG reading is low or high, or there are symptoms of low or high glucose, confirm the SG reading with a BG meter prior to making therapy decisions to avoid hypoglycemia or hyperglycemia.

- For persons seven to thirteen years of age, sensor insertion is approved for in the abdomen and buttocks. Do not insert the sensor into any other location.
- For persons fourteen years and older, sensor insertion is approved for the abdomen and back of the upper arm. Do not insert the sensor into any other location.

11.3. Potential Benefits

Subjects' participation in this study may offer no additional benefits in respect to the same treatment provided outside of the trial. Participation in this study will help in contributing to evidence-based medicine and in releasing data to support product reimbursement and utilization in France.

11.4. Risk-Benefit Rationale

Subjects are not put at any additional risk for participating in the study, as compared having the MiniMed™ 780G System treatment as part of their routine care.

The probable benefits of the device are based on data collected in several clinical research studies as described in section 4.1 Background. These data are and were used to support regulatory approval of the MiniMed™ 780G System in the United States and in Europe.
Participation in this study will help in contributing to evidence-based medicine and in releasing data to support product reimbursement and utilization in France.

12. Statistical Design and Methods

12.1. Sample size justification

The primary endpoint is to evaluate if the MiniMed™ 780G therapy in Auto Mode increases the proportion of Time In Range (TIR) at 6 months compared to the MiniMed™ 780G therapy in manual mode at baseline. The endpoint is the Time In Range (TIR) defined as the proportion of sensor glucose concentration within the target range 70-180 mg/dL (3·9–10·0 mmol/L).

The Pivotal study [12, 13] enrolled adolescents (ages 14–21 years) and adults (ages 22–75 years) with type 1 diabetes in a multicenter pivotal trial. The Medtronic MiniMed™ 670G system was used during a 2- week run-in phase without HCL control, or Auto Mode, enabled (Manual Mode) and, thereafter, with Auto Mode enabled during a 3-month study phase. The study has shown a significant

improvement on TIR of 60.4% (10.9%) to 67.2% (8.2%) in adolescents and from 68.8% (11.9%) to 73.8% (8.4%) in adults. Using this information and considering that this study is expected to include around 32 sites and including also patients aged >7 years old, a lower increase of TIR and higher variability are expected. The following assumptions were made:

- Improvement in TIR of at least 3% points at 6 months compared to the baseline.
- Standard deviation as 16% due to the mixed population and multiple sites expected for this study.

12.2. Sample size Calculations

The sample size was determined using a one sample paired test assuming a one-sided type I error rate of 0.05 and a power greater than 90%. The TIR at baseline is assumed to be 60% and the TIR at 6 months follow up (TIR calculated using overall 6 months CGM data) is assumed to be 63% with same standard deviation as 16% and a correlation as 0.5. Thus, the hypothesis to be tested is:

$H0: \mu TIR6m - \mu TIR\ baseline = d0$

$HA: \mu TIR6m - \mu TIR\ baseline > d0$

where d0 = 3 is the expected increase of TIR at 6 months. The sample size needed to demonstrate this hypothesis is 245 paired assessments per subject. The calculation is adjusted for loss-to-follow-up and protocol failures, including potential subjects with less than 70% of the time in Auto Mode with an assumption considering an attrition rate of 20%. The total number of subjects to be enrolled is 306.

12.3. Data Analysis

A detailed description of the statistical methods will be contained in the Statistical Analysis Plan (SAP). Any change to the data analysis methods described in this section and/or the SAP will require an amendment only if it changes a principal feature of the study description. Any other changes to the data analysis methods will be described and justified in the Final Report or publications.

Descriptive statistics will be used to summarize patient characteristics. For categorical variables, the description will consist at least of the sample size, numbers of missing data and valid data, the frequency and the percentage of each category. Denominators for calculation of percentages will be taken as the number of subjects with available (not missing or unknown) observations in the specified patients sets and groups unless otherwise stated. Percentages will be presented with no decimal. For continuous variables, the description will consist at least of the sample size (N), number of subjects with non-missing observation (n), mean, standard deviation, standard error, minimum,

median and maximum. For n<3, only mean, minimum and maximum will be displayed. In general, minimums and maximums will be presented to the same level of accuracy as the raw data; means and medians will be presented to 1 further decimal place; if appropriate, standard deviation and standard error will be presented to 2 further decimal places.

Since the impact of missing data is expected to be small no multiple imputation method for missing data is planned. However, should the issue of missing data arise, the choice of the imputation method for missing data will depend on the pattern of missing data and the type of the imputed variable.

The study is a multicenter trial and a multicenter impact on primary outcomes will be investigated. A description by means summary statistics on primary outcomes by sites will be provided.

Outliers and influential observations will be identified via graphical plots. Once outliers or influential observations are identified, the study team will be informed and according to their decision the analysis for primary endpoint may be repeated excluding the outliers. Additional exploratory analyses will be conducted as deemed appropriate.

The primary analysis will be performed on the Intention To Treat (ITT) set and a sensitivity analysis will be performed using the Per Protocol set including all subjects that were compliant with the protocol.

The ITT includes all patients enrolled in the study those sign Data Release Form, fulfill the inclusion and exclusion criteria. The ITT will be used for all endpoints and safety evaluation. For patients who dropout the analyses will include all data up to the point of their last data collection.

The PP includes all patients enrolled in the study those sign Data Release Form, fulfill the inclusion and exclusion criteria and having at least 70% of time using the Auto Mode. The PP set will be used for all endpoints.

The primary endpoint on efficacy defined as the change of TIR at 6 months from Auto Mode activation at baseline will be analyzed by means of paired (samples) t-test or Wilcoxon signed rank sum test according to the normal or non-normal distribution. The mean change will be displayed together with their 95% confidence interval (95%CI). Additional exploratory analysis on the TIR change over time (baseline, 3, 6 and 12 months follow-up) will be analyzed by means of mixed models for repeated measures. The dependent variable will be pre-log transformed depending on normal or non-normal distribution. The model will have the clinical outcomes as dependent variables and baseline values and visits as explanatory variables. All assumptions for regression models will be performed by assessment of plots of the residual values. Difference between visits means will be tested by applying contrast on the estimated model. The plot for the mean change over time will be

reported.

The secondary endpoint on satisfaction defined by the DTSQc will be analyzed by means of one sample Z- score test. The DTSQc has six items related to treatment satisfaction and two other items assess perceived frequency of hyperglycemia and hypoglycemia. Each item has a maximum of 3 (more satisfied now) and a minimum of -3 (less satisfied now) with a midpoint of 0 reflecting no change. The scale total is computed by adding 6 items (1,4,5,6,7,8) and the 2 items on hypo/hyperglycemia will be analyzed separately. Previous studies on patients treated with MiniMed™ 640G pump have shown a good satisfaction using the DTSQc questionnaire. The sample size estimated would also allow us to demonstrate a positive DTSQc satisfaction score.
Other secondary endpoints on quality of life defined as the change from baseline will be analyzed by means of paired (samples) t-test or Wilcoxon signed rank sum test according to the normal or non-normal distribution. The mean change will be displayed together with their 95% confidence interval (95%CI).
The secondary endpoint on HbA1c change over time (baseline, 6- and 12-months follow-up) will be analyzed by means of mixed models for repeated measures. The dependent variable will be pre-log transformed depending on normal or non-normal distribution. The model will have the clinical outcomes as dependent variables and baseline values and visits as explanatory variables. All assumptions for regression models will be performed by assessment of plots of the residual values. Difference between visits means will be tested by applying contrast on the estimated model. The plot for the mean change over time will be reported.

It is anticipated that SAS (SAS Institute Inc., Cary, NC, USA) will be used to perform all statistical analyses. Statistical tests will be based on a one-sided significance level of 0.05, and possible interaction effects will be evaluated at a significance level of 0.10. No adjustments for multiple comparisons will be performed. Additional exploratory analyses will be conducted as deemed appropriate.

Procedures for reporting any deviation(s) from the original statistical plan including that justification will be documented.

13. Ethics

13.1. Statement(s) of Compliance

The study is designed to reflect the Good Clinical Practice (GCP) principles such as the protection of the rights, safety and well-being of human subjects, controls to ensure the scientific conduct and credibility of the clinical investigation and the definition of responsibilities of Medtronic and investigators.

The study will be conducted according to national and local laws, regulations, standards and requirements of the country in which the clinical study is conducted, including data protection laws, and according to the Clinical Investigation Agreement and the Clinical Investigation Plan.

The study will also be conducted in compliance with the latest version of the Declaration of Helsinki. The principles of the Declaration of Helsinki are implemented in this study by means of the patient Data Release Form (DRF) process, Ethics Committee approval, study training, clinical trial registration and publication policy.

Where applicable, regulatory authority notification will be done. Investigational sites will not be activated, nor begin enrolling subjects, until the required approval/favorable opinion from the respective Ethics Committee has been obtained (as appropriate).

Additionally, any requirements imposed by the regulatory agency or Ethics Committee shall be followed, as appropriate. Medtronic will be informed by the Ethics Committee and/or the investigator in case any action is taken by an Ethics Committee with respect to this investigation.

14. Study Administration

14.1. Monitoring

Monitoring and monitoring oversight will be provided by Medtronic and detailed in a study-specific Monitoring Plan separate from this CIP. The list of monitors involved in the study will be maintained under a separate cover.

Site qualification will be conducted by Medtronic personnel remotely to verify site interest and capability to perform the study. Prior to first enrollment Medtronic will conduct training to prepare the site to conduct the study, as outlined in the Monitoring Plan. In addition, monitoring visits will be conducted during the course of the study in accordance with Medtronic Standard Operating Procedures (SOPs) and the Monitoring Plan.

Regulatory documents (e.g. EC approval letter and Clinical Trial Agreement) will be reviewed, a complete list of documents that will be reviewed is maintained in the Monitoring Plan. Subject data will be monitored against source documentation (e.g. clinic and hospital charts) as specified in the Monitoring Plan. Extent of source data verification will also be detailed in the Monitoring Plan and performed accordingly. Center study progress, investigator's adherence to the CIP and maintenance of records and reports will be checked.

The principal investigator(s) or his/her delegate(s) shall be accessible to Medtronic study team. This

accessibility is of particular importance for reviewing data in the eCRF.

Direct access to patient medical files for source data verification should be granted and prepared prior to any monitoring visits. If electronic source documentation is used at the site, the site must provide to the monitor:

- Direct access to the electronic medical record(s), or
- Direct access to the electronic medical record(s) by reviewing alongside appropriate study staff.

Findings from each monitoring visit will be provided in writing to the clinical study personnel at the site. Corrective action will be taken to resolve any issues of noncompliance.

14.2. Data Management

Data will be collected using an electronic data management system for studies. CRF data will be stored in a secure, password-protected database which will be backed up nightly. Data will be reviewed using programmed and manual data checks. Data queries will be made available to study sites for resolution. Study management reports may be generated to monitor data quality and study progress. At the end of the study, the data will be frozen and will be retained indefinitely by Medtronic.

All records and other information about subjects participating in this study will be treated as confidential. Data will be transferred and processed by Medtronic or a third party designated by Medtronic in a key coded form, unless it's impossible to pseudonymize for instance.

Procedures in the CIP require source documentation. Source documentation will be maintained at the study site. Source documents, which may include worksheets, subject medical records, programmer printouts, and interrogation files, must be created and maintained by the investigational study site team.

The investigator must ensure accuracy, completeness and timeliness of the data reported in the eCRFs and in all other required reports, if any. Electronic device data will be collected from the study pump using CareLink™ Personal For Clinical Research software. The system uses TLS technology, which encrypts all data it stores.

Only authorized persons can complete eCRFs. eCRFs shall be signed by investigators (physicians only) as specified on the Delegated Tasks List included in the Investigator Site File. If a person is only authorized to complete eCRFs or make changes to an already signed eCRF, the investigator shall re-sign this eCRF.

The RDC system maintains an audit trail on entries, changes or corrections in the eCRFs. The study database will employ validation programs (e.g. range and logic checks) on entered data to identify possible data entry errors and to facilitate data validation.

A copy of the electronic Case Report Forms will be provided under a separate cover.

It is expected that eCRF will be completed within 10 working days from the performed visit or as soon as source documents are available. A delayed completion of the eCRF will not be considered a Protocol Deviation.

Data management will be done according to Medtronic SOPs and the Data Management Plan for this study. These documents will be made available upon request.

Data will be reviewed for completeness, correctness and consistency. In case of issues, queries will be sent to the investigator to complete, correct or comment the data.

14.3. Direct Access to Source Data/Documents

The PI and the study team must ensure availability and accessibility of source documents from which the information on the eCRF was derived to Medtronic personnel, monitoring team and clinical study manager. This accessibility is of particular importance for reviewing data in the CRF.

In addition to monitoring visits, Medtronic may conduct audits at participating investigational sites. The purpose of an audit is to verify the adequate performance of the clinical study related activities. Regulatory authorities may also perform inspections at participating investigational sites.

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

Any regulatory authority inspection announcements shall be forwarded immediately to the Clinical Study Team.

14.4. Confidentiality

All information and data sent to parties involved in study conduct concerning subjects or their participation in this study will be considered confidential. Each enrolled subject will be assigned to a unique subject ID number (SID), which is pre-configured in EDC system. Records of the subject/SID relationship will be maintained by the study site. The SID is to be recorded on all study documents to link them to the subject's medical records at the site. To maintain confidentiality, the subjects' name or any other personal identifiers should not be recorded on any study document other than the

subject's DRF. In the event a subject's name is included for any reason, it will be immediately blinded as applicable.

Confidentiality of data will be observed by all parties involved at all times throughout the clinical study. All data shall be secured against unauthorized access. The privacy of each subject and confidentiality of his/her information shall be preserved in reports and when publishing any data.

Sites will maintain subject privacy according to local and national regulations and institutional requirements.

In general Sponsor's representatives, EC members, European or other international public regulatory authorities may have access to subject confidential information.

14.5. Liability

Due to the study type, no insurance is needed in accordance with local law. However, Medtronic maintains a General Liability Insurance Coverage, including products. If required, a General Liability Insurance statement could be provided. Warranty information is provided in the product packaging for the commercially released MIniMed 780G system and additional copies are available upon request.

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

14.6. CIP Amendments

In case the investigator proposes any appropriate modification(s) of the CIP or product use, Medtronic will review this proposal and decide whether the modification(s) will be implemented.

Medtronic will submit any significant amendment to the CIP, including a justification for this amendment, to the appropriate EC and to the investigators. The investigator will only implement the amendment after approval of the EC and sponsor. Furthermore, investigators shall sign any approved amendment for agreement.

14.7. Records and reports

14.7.1. Investigator Records

The investigator is responsible for the retention of the records listed below. The Investigator Site File or appropriate Patient Study Binders shall include at a minimum the following records:

- Clinical Investigation Plan and, if applicable, any amendment
- Signed and dated Clinical Investigation Agreement
- Instructions For Use
- Completed Subject Identification log for all enrolled patients
- Blank Patient Data Release Form
- Delegated Tasks List
- Training documentation of study site personnel
- Dated current CV of the study site personnel
- Study-related correspondence between center and sponsor
- Patient questionnaires
- Signed Patient Data Release Form

14.7.2. Investigator reporting responsibilities

The investigator is responsible for completing and signing off all electronic case report forms, for study deviation reporting through the electronic Case Report Forms. If any action is taken by an EC with respect to this study, copies of all pertinent documentation must be forwarded to Medtronic in a timely manner.

14.7.3. Sponsor Records

The sponsor is responsible for the retention of the records listed below. The Trial Master File shall include at a minimum the following records:

- All documents and correspondence which pertains to the trial
- Clinical Investigation Plan and, if applicable, any amendments
- List of participating centers
- Relevant correspondance with the Haute Autorité de Santé (HAS), if any
- Names/contact addresses of study monitors
- Statistical analyses and underlying supporting data
- Final report of the clinical investigation
- Signed and dated Clinical Investigation Agreements for all centers
- Instructions For Use
- Blank Patient Data Release Form
- Training documentation of site personnel involved in the study

- All Delegated Tasks Lists
- Dated current CV of all investigators (dated less than 3 years before site activation)
- All reports related to study monitoring activity
- Fully completed e-CRFs
- Any other document that the HAS may require to be maintained

14.7.4. Sponsor reporting requirements

Medtronic shall prepare and submit the following complete, accurate, and timely reports listed in the Table 5. In addition to the reports listed below, Medtronic shall, upon request of Competent Authorities provide accurate, complete and current information about any aspect of the study.

Table 5: Sponsor reporting requirements

Report	Submit to	Description
Premature termination or suspension of the study	Investigators, reviewing EC	Medtronic will provide prompt notification of termination or suspension and reason(s) to investigators. Medtronic will inform the reviewing EC.
Incident/Risk of Incident Withdrawal of device from market	Competent Authority	Medtronic will immediately inform Competent Authority if not already done by investigators.
Subject enrollment complete	Investigators	Medtronic will notify the investigators as soon as possible of the completion of the enrollment.
Statistical analysis plan	HAS	Medtronic will submit the statistical analysis plan, including analysis scheduled for each endpoint, before the analyses are performed.
Interim Report	HAS	Medtronic will submit the interim report of the study to HAS 6 months before the renewal deadline.
Final report	Investigators, and the HAS	Medtronic will provide investigators and the HAS with a copy of the final report of the study. Final study report must be available for ANSM in case of request

14.7.5. Record Retention

Medtronic records and reports will be stored at Medtronic during the course of the study. After the closure of the study, all records and reports will be archived per Medtronic standards.

The investigator must be willing to give access to study monitors, auditors, EC members and inspectors, and have appropriate facilities to retain relevant study documents. The investigator must retain the Investigator Site File, patient source documents and CRFs for a minimum of 15 years after study closure or longer if required by local law, regulations or institution.

The investigator and sponsor must take measures to prevent accidental or early destruction of the study related materials. No study document or image will be destroyed without prior written agreement between Medtronic and the investigator. Should the investigator wish to assign the study records to another party or move them to another location, advance written notice must be given to Medtronic.

14.8. Publication and Use of Information

The study will be registered in a public database.
Publications and presentations referring to this clinical study will be coordinated by Medtronic to allow the use of all available data.

All participating investigational sites will have to adhere to the following Publication Policy:

- Medtronic may use the study data for regulatory authority submission, may publish the results in peer reviewed scientific journal(s) and present the data at major congresses.
- Authorship on any publication(s) resulting from this clinical study will be assigned according to substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data, drafting the article or revising it critically for important intellectual content, and final approval of the version to be published. This is in accordance with the Vancouver principles (The Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication, ICMJE, October 2008), as agreed upon by the editors of all major medical journals.
- The number of authors will be dependent on the regulations of the concerning journal. Names of all participating investigators will appear in the Acknowledgment of the paper, if allowed by the journal.
- Based on the principle that Medtronic owns the data of this clinical study, a single investigational site may access and use the data provided by itself for scientific publications following prior approval by Medtronic.
- Pooling data from several investigational sites for publication purposes, national projects and international projects all require prior approval from Medtronic.

- Medtronic as the owner of the data can use the data and/or any results derived from the data or publications based on that data for marketing purposes, further research and development of devices or educational use.

The study sponsor will collect data in such way that no subject can be identified. Participating subjects will not be identified by name in any published reports about the clinical study.

14.9. Suspension or Early Termination

14.9.1. Early study suspension or termination

Early Termination is the closure of a study that occurs prior to meeting defined endpoints. This is possible for the whole study or a single study site Suspension is a temporary postponement of study activities related to enrollment and distribution of the product Medtronic may decide to suspend or prematurely terminate the study (e.g. if information becomes available that the risk to study subject is higher than initially indicated). If the study is terminated prematurely or suspended, Medtronic shall promptly inform the clinical investigators and the reviewing EC of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform the study subjects. The clinical research agreement will be amended or terminated.
Possible reasons for considering study-wide suspension or termination of the study include but are not limited to:

- New findings associated with the system or product under investigation which might be related to the safety or welfare of the subject
- Observed/suspected performance different from the product's design intent
- Decision by Medtronic
- Technical issues during the manufacturing process

14.9.2. Early investigational site suspension or termination

Medtronic or EC may decide to suspend or prematurely terminate an investigational site. If an investigational site is suspended or prematurely terminated, Medtronic shall promptly inform the investigator(s) and the reviewing EC of the termination or suspension and the reason(s) for this. The investigator shall then promptly inform 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 site and immediately inform the sponsor and EC, if applicable.

Possible reasons for clinical investigator or center termination or suspension include but are not limited to:

- Consistent non-compliance to the CIP (e.g. failure to adhere to inclusion/exclusion criteria, failure to follow subjects per scheduled follow-ups, etc.)
- Lack of enrollment
- Noncompliance to regulations and the terms of the Clinical Study Agreement (e.g. failure to submit data in a timely manner, failure to follow-up on data queries and monitoring findings in a timely manner, etc.)
- Ethics Committee suspension of the center
- Fraud or fraudulent misconduct (as defined by local law and regulations)
- Investigator request (e.g. no longer able to support the study)

14.9.3. Subject follow-up in case of termination

In case of early termination and at study exit, all subjects should continue to be followed by their physicians per standard care and no further patient data will be collected under this clinical investigation plan.

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16. Version History

Version	Summary of Changes	Author(s)/Title
1.0	Initial release	[redacted] Prin Project and Clinical Research Spec.
2.0	• Replaced "to demonstrate" with "to evaluate" in the Primary Objective; • Included details related to patient selection and informed consent process in the enrollment/baseline section; • Adjusted total site number throughout the document; • Added study duration in the synopsis; • Clarified use of different questionnaire versions per age groups regarding DQOL and HFS; • Specified subject should be under CSII therapy in inclusion criterion #4; • Adjusted typos and inconsistencies.	[redacted] Sr. Clinical Research Specialist
3.0	• Specified in exclusion criteria #2 and #3 period for which patients that have been using pumps with predictive algorithms (PLGM or LGS) are to be excluded: in the last 6 months before recruitment. • Added Auto Mode activation in baseline visit to clarify study phase period start date • Adjusted Carelink™ data upload recurrence • Adjusted typos and inconsistencies, general corrections in spelling and grammar.	[redacted] Clinical Research Specialist
4.0	• Adjusted typos and inconsistencies, general clarifications and grammatical changes • Replaced "MiniMed™ 670G" with "MiniMed™ 780G" throughout the document • Updated table of contents • Adjusted list in the Glossary • Updated list of Product Name • Added HbA1c data collection at 6 months and 12 months. Added "the change in HbA1c from baseline to 6 months and 12 months" in the Secondary Objective and Secondary Endpoint. Added information on the HbA1c in Section 12.3 Data Analysis • Updated the TIR standard deviation and the sample size throughout the document	[redacted] Clinical Research Specialist

	• Updated Carelink Personal for Clinical Research connectivity throughout the document • Updated Background Section and moved paragraph on HCL technology from Section 6.1 Rational to Background • Updated Table 1, 2, 3, 4 • Updated Figure 1, 3, 6. Added Figure 8, 9 • Updated or added Sections 4.2, 6, 7.1, 7.6, 7.7, 7.8, 8, 10, 11.2, 14.2, 14.5, 14.7.5, 14.9.1 due to GAP analysis between new CIP Template 056-F275 v.B and v.A • Moved information on Site and Investigator selection, clinical investigational agreement and curriculum vitae from Section 10 to Section 8 due to GAP analysis between CIP Template 056-F275 v.B and v.A • Added the Sub-Section 11.2 Risk Minimization due to GAP analysis between CIP Template 056-F275 v.B and v.A • And moved information on Specific Rosks from Section 11.1 to 11.2 due to GAP analysis between CIP Template 056-F275 v.B and v.A • Added information on The Hypoglycemia Fear Survey, Section 6.1 • Updated the Section 7 Product Description. Moved paragraph on Glucose Sensor from Background and added the Sub-Sections for: Accu-Chek® Guide Link Blood Glucose Meter, MiniMed Mobile App Patients, CareLink™ BLE USB [Blue Adaptor], Product Accountability • Updated Data Analysis “use ITT as a primary dataset and PP as a sensitivity analysis dataset” in Section 12.3 and throughout the document • Updated References	