SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Automated Insulin Dosing System

Device Trade Name: MiniMed 780G System

Device Procode: OZP

Applicant's Name and Address: Medtronic MiniMed, Inc.
18000 Devonshire Street
Northridge, CA 91325

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P160017/S091

Date of FDA Notice of Approval: 4/21/2023

The original PMA for the MiniMed 670G system (P160017) was approved on September 28, 2016, for use in persons ages 14 years and older. PMA Panel Track Supplement P160017/S017, approved on February 13, 2018, added the upper arm as an alternate insertion site for the Guardian Sensor (3). PMA Panel Track Supplement P160017/S031, approved on June 21, 2018, expanded the indication for pediatric patients 7 to 13 years of age. PMA Panel Track Supplement P160017/S076, approved on August 31, 2020, expanded the indications for the MiniMed 770G system to include pediatric patients down to 2 years old and changed the pump communication protocol to Bluetooth Low Energy (BLE).

The current Panel Track Supplement was submitted to introduce the MiniMed 780G System, which updates the pump control algorithm from the Hybrid Closed Loop (HCL) algorithm to the Advanced Hybrid Closed Loop (AHCL) algorithm and to add compatibility to the new Guardian 4 Continuous Glucose Monitor (CGM) as an alternative CGM component for the system.

II. INDICATIONS FOR USE

The MiniMed 780G system is indicated for use with either the Guardian Sensor (3)/Guardian Link (3) Transmitter, or with the Guardian 4 sensor/Guardian 4 transmitter Indications for use for the MiniMed 780G system are provided for each of the two system configurations separately:

MiniMed 780G System for use with Guardian Sensor (3)/Guardian Link (3) Transmitter

MiniMed 780G System
The MiniMed 780G system is intended for continuous delivery of basal insulin at selectable rates, and the administration of insulin boluses at selectable amounts for the management of type 1 diabetes mellitus in persons seven years of age and older requiring insulin. The system is also intended to continuously monitor glucose values in the fluid under the skin. The MiniMed 780G system includes SmartGuard (SG) technology, which can be programmed to automatically adjust insulin delivery based on continuous glucose monitoring (CGM) sensor glucose values and can suspend delivery of insulin when the SG value falls below or is predicted to fall below predefined threshold values.

The MiniMed 780G system consists of the following devices:

- MiniMed 780G insulin pump
- Guardian Link (3) transmitter
- Guardian Sensor (3)
- One-press serter
- Accu-Chek™ Guide Link blood glucose meter
- Accu-Chek™ Guide Test Strips

The system requires a prescription from a healthcare professional.

Guardian Sensor (3)
The Guardian Sensor (3) is intended for use with the MiniMed 780G system, MiniMed 770G system, MiniMed 670G system, MiniMed 630G system, and Guardian Connect system to continuously monitor glucose levels in persons with diabetes.

The sensor is intended for single use and requires a prescription. The Guardian Sensor (3) is indicated for seven days of continuous use.

The Guardian Sensor (3) is not intended to be used directly to make therapy adjustments while the MiniMed 780G system is operating in manual mode. All therapy adjustments in manual mode should be based on measurements obtained using a blood glucose meter and not on values provided by the Guardian Sensor (3).

The Guardian Sensor (3) has been studied and is approved for use in the systems, insertion sites, and ages listed in the following table:

System	Approved Age	Sensor Insertion Site
MiniMed 780G system	7- 13 14 and older	Abdomen and Buttocks Abdomen and Arm
MiniMed 770G system	2-13 14 and older	Abdomen and Buttocks Abdomen and Arm

System	Approved Age	Sensor Insertion Site
MiniMed 670G system	7-13 14 and older	Abdomen and Buttocks Abdomen and Arm
MiniMed 630G system	14 and older	Abdomen and Arm
Guardian Connect system	14 and older	Abdomen and Arm

One-press Serter
The serter is used as an aid for inserting the sensor. It is indicated for single-patient use and it is not intended for multiple-patient use.

Guardian Link (3) Transmitter
The Guardian Link (3) Transmitter is intended for use with the MiniMed 780G system. The Guardian Link (3) Transmitter powers the glucose sensor, collects and calculates sensor data, and wirelessly sends the data to the MiniMed 780G insulin pump. The transmitter is intended for single-patient multi-use.

Accu-Chek™ Guide Link Blood Glucose Monitoring System
The Accu-Chek™ Guide Link Blood Glucose Monitoring System is comprised of the Accu- Chek™ Guide Link meter and the Accu-Chek™ Guide test strips.

The Accu-Chek™ Guide Link Blood Glucose Monitoring System is intended to quantitatively measure glucose in fresh capillary whole blood from the fingertip, palm, and upper arm as an aid in monitoring the effectiveness of glucose control.

The Accu-Chek™ Guide Link Blood Glucose Monitoring System is intended for *in-vitro* diagnostic single-patient use by people with diabetes.

The Accu-Chek™ Guide Link Blood Glucose Monitoring System is intended to be used by a single person and should not be shared.

This system is not for use in diagnosing or screening for diabetes mellitus and not for neonatal use.

Alternative site testing should be done only during steady-state times (when glucose is not changing rapidly).

The Accu-Chek™ Guide Link Blood Glucose Monitoring System is intended to be used to wirelessly transmit glucose values to the MiniMed 780G system and MiniMed 770G system with Bluetooth wireless technology through the use of Bluetooth low energy communication.

MiniMed 780G System for use with Guardian 4 Sensor/Guardian 4 Transmitter

MiniMed 780G System
The MiniMed 780G system is intended for continuous delivery of basal insulin at selectable rates, and the administration of insulin boluses at selectable amounts for the

management of type 1 diabetes mellitus in persons seven years of age and older requiring insulin. The system is also intended to continuously monitor glucose values in the fluid under the skin. The MiniMed 780G system includes SmartGuard (SG) technology, which can be programmed to automatically adjust insulin delivery based on continuous glucose monitoring (CGM) sensor glucose values and can suspend delivery of insulin when the SG value falls below or is predicted to fall below predefined threshold values.

The MiniMed 780G system consists of the following devices:

- MiniMed 780G insulin pump
- Guardian 4 transmitter
- Guardian 4 sensor
- One-press serter
- Accu-Chek™ Guide Link blood glucose meter
- Accu-Chek™ Guide Test Strips

The system requires a prescription from a healthcare professional.

Guardian 4 Sensor
The Guardian 4 Sensor is intended for use with the MiniMed 780G system and the Guardian 4 transmitter to continuously monitor glucose levels for the management of diabetes.

The sensor is intended for single use and requires a prescription. The Guardian 4 sensor is indicated for up to seven days of continuous use.

The Guardian 4 sensor is not intended to be used directly to make therapy adjustments while the MiniMed 780G is operating in manual mode. All therapy adjustments in manual mode should be based on measurements obtained using a blood glucose meter and not on values provided by the Guardian 4 sensor.

The Guardian 4 sensor has been studied and is approved for use in the systems, insertion sites, and ages listed in the following table.

System	Age	Sensor Insertion Site
MiniMed 780G system	7 years and older	Arm

One-press Serter
The serter is used as an aid for inserting the sensor. It is indicated for single-patient use and it is not intended for multiple-patient use.

Guardian 4 Transmitter
The Guardian 4 transmitter is intended for use with the MiniMed 780G system and Guardian 4 sensor to monitor glucose levels for the management of diabetes.

Accu-Chek™ Guide Link Blood Glucose Monitoring System

The Accu-Chek™ Guide Link Blood Glucose Monitoring system is comprised of the Accu- Chek™ Guide Link meter and the Accu-Chek Guide test strips.

The Accu-Chek™ Guide Link Blood Glucose Monitoring System is intended to quantitatively measure glucose in fresh capillary whole blood from the fingertip, palm, and upper arm as an aid in monitoring the effectiveness of glucose control.

The Accu-Chek™ Guide Link Blood Glucose Monitoring System is intended for *in-vitro* diagnostic single-patient use by people with diabetes.

The Accu-Chek™ Guide Link Blood Glucose Monitoring System is intended to be used by a single person and should not be shared.

This system is not for use in diagnosing or screening for diabetes mellitus and not for neonatal use.

Alternative site testing should be done only during steady-state times (when glucose is not changing rapidly).

The Accu-Chek™ Guide Link Blood Glucose Monitoring System is intended to be used to wirelessly transmit glucose values to the MiniMed 780G system and MiniMed 770G system with Bluetooth wireless technology through the use of Bluetooth low energy communication.

III. CONTRAINDICATIONS

MiniMed 780G System for use with Guardian Sensor (3)/Guardian Link (3) Transmitter

A prominent boxed warning is included in the labeling regarding use of the device by users with a total daily insulin dose of less than 8 units:
"Do not use the SmartGuard feature for people who require less than eight units or more than 250 units of total daily insulin per day. A total daily dose of at least eight units, but no more than 250 units, is required to use the SmartGuard feature."
The following contraindications for this device are also described in the labeling:

- Pump therapy is not recommended for people whose vision or hearing does not allow for the recognition of pump signals, alerts, or alarms.
- Do not use the serter to insert sensors other than the Guardian Sensor (3). Medtronic cannot guarantee the safety or efficacy of this product if used with other sensors.
- The reservoir is contraindicated for the infusion of blood or blood products.
- Infusion sets are indicated for subcutaneous use only and not for intravenous (IV) infusion.
- Infusion sets are not indicated for the infusion of blood or blood products.
- Insulin pump therapy is not recommended for those who are unwilling to perform at least four BG meter readings per day. As insulin pumps use rapid-acting insulin only, BG testing is required to help identify rapid glycemic

deterioration due to insulin infusion occlusion, infusion site problems, insulin stability issues, user error, or a combination of these.
- Pump therapy is not recommended for people who are unwilling or unable to maintain contact with their healthcare professional.

MiniMed 780G System for use with Guardian 4 Sensor/Guardian 4 Transmitter

A prominent boxed warning is included in the labeling regarding use of the device by users with a total daily insulin dose of less than 8 units:

"Do not use the SmartGuard feature for people who require less than eight units or more than 250 units of total daily insulin per day. A total daily dose of at least eight units, but no more than 250 units, is required to use the SmartGuard feature."

The following contraindications for this device are also described in the labeling:

- Pump therapy is not recommended for people whose vision or hearing does not allow for the recognition of pump signals, alerts, or alarms.
- Do not use the serter to insert sensors other than the Guardian 4 sensor. Medtronic cannot guarantee the safety or efficacy of this product if used with other sensors.
- The reservoir is contraindicated for the infusion of blood or blood products.
- Infusion sets are indicated for subcutaneous use only and not for intravenous (IV) Infusion.
- Infusion sets are not indicated for the infusion of blood or blood products.
- Insulin pump therapy is not recommended for persons who are unwilling to perform BG meter readings.
- Pump therapy is not recommended for people who are unwilling or unable to maintain contact with their healthcare professional.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the MiniMed 780G system labeling.

V. DEVICE DESCRIPTION

The MiniMed 780G system is similar to the MiniMed 770G system (approved under P160017/S076). The Hybrid Closed Loop algorithms approved under P160017 were modified to the Advanced Hybrid Closed Loop (AHCL) algorithms. The MiniMed 780G system includes the following additional features that were not part of the MiniMed 770G system:

- Auto Correction Bolus Feature – A new feature that delivers correction boluses automatically under specific conditions without any user input or acknowledgement.
- Adjustable Target Setpoints – The Auto Basal Rate can be adjusted to one of 3 target setpoints: 100 mg/dL, 110 mg/dL or 120 mg/dL.
- Finetuning of Safeguards – Incorporated to reduce Auto Mode exits.
- User Interface Enhancements – Several screens updated and redesigned to clarify messaging for completing pump tasks.

The MiniMed 780G system is comprised of the following devices:

MiniMed 780G Pump (MMT-1884)

The MiniMed 780G pump (model MMT-1884) is an ambulatory, battery-operated, rate-programmable micro-infusion pump designed to deliver insulin from a reservoir. The reservoir is driven by a motor to deliver pre-determined basal rate profiles and user-selected bolus amounts of insulin into the subcutaneous tissue through an infusion set.

The MiniMed 780G pump is offered in one model (MMT-1884). The pump houses electronics, a pumping mechanism, a user interface, and a medication reservoir within the same physical device. The reservoir is attached to a tube that connects to the user's infusion site on their body. The pump is intended to deliver insulin through a diffusion mechanism. Model MMT-1884 is compatible with a 3.0 mL reservoir. The pump only displays blood glucose level units in mg/dL and this units setting cannot be reconfigured by the user.

In addition to insulin delivery, the MiniMed 780G pump is designed to receive and display real-time interstitial fluid glucose values from a compatible CGM. The pump is compatible with two CGMs: the Guardian Sensor (3) with Guardian Link (3) Transmitter, and the Guardian 4 sensor with Guardian 4 transmitter. When used in combination with a CGM, the transmitter sends sensor signals to the MiniMed 780G pump via a BLE wireless communication protocol every five minutes.

When using the 780G pump with the Guardian Sensor (3), a BG meter reading is required at least every 12 hours to calibrate the sensor for optimal sensor performance. When using the 780G pump with the Guardian 4 sensor, calibration is not required. However, the system is designed to use every BG meter reading either entered manually or received from a linked glucose meter to calibrate the sensor.

The 780G Pump can operate in Manual Mode or Auto Mode, and each mode includes various features and capabilities. These features and capabilities are described in detail in the MiniMed 780G system user guide. A summary of these features and capabilities is provided in Table 1 below.

Table 1: ***Summary of the Features of the MiniMed 780G System***

Mode	Description	When is it Active?	Will I receive Alerts?
Manual Mode: Insulin Infusion Pump	This mode is when the device is functioning as a pump that can deliver insulin, but the device does not have a sensor connected, is not in Auto Mode and the insulin suspend features are not turned on.	This is the default mode and the user does not have to specifically turn this mode on.	There are alerts if the pump has any issues with delivering insulin (e.g. suspended delivery) or low reservoir.

Mode	Description	When is it Active?	Will I receive Alerts?
Manual Mode: Sensor Augmented Pump	This mode is when the device is functioning as a sensor and pump, but the device is not in Auto Mode and the insulin suspend features are not turned on.	The user has to be wearing a CGM that will be communicating to the pump in order to receive sensor glucose alerts.	There is a mandatory severe low alarm for the system used with each compatible CGM: 54 mg/dL Guardian Link (3) CGM; 64 mg/dL Guardian 4 CGM. The user can also set optional high and low alerts to sound on or before set sensor glucose levels.
Manual Mode: Suspend On Low	When this feature is active the device detects that your sensor glucose level has reached a pre-set sensor glucose value and it automatically suspends basal insulin delivery when that value is reached.	The user has to turn this feature on. It is not available when Auto Mode is turned on, and it cannot be turned on if Suspend before Low is turned on.	There is a mandatory severe low alarm for the system used with each compatible CGM: 54 mg/dL for the Guardian Link (3) CGM; or 64 mg/dL for the Guardian 4 CGM, and at the pre-set low level. The user can also set optional high alerts to sound on or before set sensor glucose levels, and an optional alert before low alert.
Manual Mode: Suspend Before Low	When this feature is active the device detects when your sensor glucose is predicted to reach a pre-set value and it automatically suspends basal insulin delivery before that value is reached.	The user has to turn this feature on. It is not available when Auto Mode is turned on, and it cannot be turned on if Suspend On Low is turned on.	There is a mandatory severe low alarm for the system used with each compatible CGM: 54 mg/dL for the Guardian Link (3) CGM; or 64 mg/dL for the Guardian 4 CGM, and at the pre-set low level. The user can also set optional high alerts to sound on or before set sensor glucose levels, and an optional alarm before low alert.
Auto Mode	When this mode is active, the device can automatically adjust basal insulin by increasing, decreasing, or turning off basal insulin delivery based on sensor glucose levels. The device can also automatically deliver an auto correction bolus without the user input based on the sensor glucose levels.	The user has to turn this mode on and certain pre-defined conditions have to be met.	There is a mandatory severe low alarm for the system used with each compatible CGM: 54 mg/dL for the Guardian Link (3) CGM; or 64 mg/dL for the Guardian 4 CGM, and a mandatory high alarm if user is ≥250 mg/dL for 3 hours; The user can also set optional high and low alerts to sound on or before set sensor glucose levels.

Mode	Description	When is it Active?	Will I receive Alerts?
Auto Mode: Safe Basal Delivery	When this feature is active, the device will deliver basal insulin at a patient-specific safe basal or safe basal low rate for no longer than 90 minutes. If the fault condition resolves within 90 minutes, the system will begin to automatically adjust basal insulin again. If the fault does not resolve within 90 minutes, the system will switch to Manual Mode.	This feature turns on when the system determines that either the sensor data is not adequate for Auto Mode or delivery at the minimum or maximum limit for a set amount of time has elapsed.	There is a mandatory alert before this feature turns on when the sensor glucose accuracy check fails. The user can also set optional alerts to sound before this feature turns on when minimum or maximum insulin delivery times out or when the sensor has been under- reading for too long. There is a mandatory severe low alarm for the system used with each compatible CGM: 54 mg/dL for the Guardian Link (3) CGM; or 64 mg/dL for the Guardian 4 CGM. The user can also set optional high and low alerts to sound on or before set sensor glucose levels.

Guardian Link (3) Transmitter (MMT-7911)

The Guardian Link (3) Transmitter is a portable, electrical current meter intended to process, store, and transmit glucose sensor values to the compatible insulin pump. The transmitter sends sensor glucose (SG) values and sensor integrity (SI) data from the Guardian Sensor (3) to the compatible insulin pumps via BLE wireless communication protocol. The transmitter was previously reviewed and approved under P160017/S076.

Guardian Sensor (3) (MMT-7020)

The Guardian Sensor (3) is a sterile, single-use, single patient glucose sensing component for continuous monitoring of glucose levels in the user's interstitial fluid for up to seven days. The Sensor is inserted into the subcutaneous tissue using the One-Press Serter and is taped to the user's skin. It connects to the Guardian Link (3) Transmitter, which in turn communicates with the MiniMed 780G Pump.

When making treatment decisions, such as determining insulin dose for meals, the MiniMed 780G with Guardian Sensor (3) continuous glucose monitor (CGM) values should not be used, as the CGM is not intended to be used to make such treatment decisions. The Guardian Sensor (3) is not intended to replace a blood glucose meter. Users should always use the values from a blood glucose meter for treatment decisions. Blood glucose values may differ from sensor glucose values. Using the sensor glucose readings for treatment decisions could lead to unwanted high or low blood glucose. When using the 780G pump with the Guardian Sensor (3), a BG meter reading is required at least every 12 hours to calibrate the sensor. The sensor was previously reviewed and approved under P160017.

Guardian 4 transmitter (MMT-7841)
The Guardian 4 transmitter is a portable, electrical current meter intended to process, store, and transmit glucose sensor values to the compatible insulin pump. The transmitter sends sensor glucose (SG) values and sensor integrity (SI) data from the Guardian 4 sensor to the MiniMed 780G insulin pump via BLE wireless communication protocol. The Guardian 4 transmitter does not require entry of fingerstick blood glucose measurement for calibration purposes.

Guardian 4 sensor (MMT-7040)
The Guardian 4 sensor is a sterile, single-use, single patient glucose sensing component for continuous monitoring of glucose levels in the user's interstitial fluid for up to seven days. The Sensor is inserted into the subcutaneous tissue using the One-Press Serter and is taped to the user's skin. It connects to the Guardian 4 transmitter, which in turn communicates with the MiniMed 780G Pump.

The Guardian 4 sensor does not require calibration for use with the system. However, every blood glucose (BG) meter reading either entered manually by the user or received from a paired meter is used to calibrate the sensor.

One-Press Serter
The One-Press serter is a sensor insertion device which aids the user in inserting the Guardian Sensor (3) and the Guardian 4 Sensor. The user must use the One-Press Serter in order to insert the Guardian Sensor (3) or the Guardian 4 Sensor. The serter was previously reviewed and approved under P120010/S070.

Accu-Chek Guide™ Link Blood Glucose Meter
The Accu-Chek Guide™ Link Blood Glucose Meter can be used with the MiniMed 780G system. The meter sends blood glucose values to the insulin pump for sensor calibration via a BLE wireless communication protocol. The blood glucose meter was previously reviewed and approved under P160017/S076.

Additional System Accessories
The following additional accessory devices listed in Table 2 are compatible with the MiniMed 780G Insulin Pump:

Table 2: Accessory Devices

Device	Model
Reservoirs and Infusion Sets	**Model Numbers**
MiniMed Quick Set infusion set	MMT-386, MMT-387, MMT-394, MMT-396, MMT-397, MMT-398, MMT-399
MiniMed Silhouette infusion set	MMT-368, MMT-377, MMT-378, MMT-381, MMT-382, MMT-383, MMT-384
MiniMed Mio Infusion set	MMT-921, MMT-923, MMT-925, MMT-941, MMT-943, MMT-945, MMT-965, MMT-975
MiniMed Sure-T infusion set	MMT-862, MMT-864, MMT-866, MMT-874, MMT-876, MMT-884, MMT-886

Device	Model
MiniMed Mio Advance infusion set	MMT-213A, MMT-242, MMT-243A, MMT-244A
Medtronic Extended infusion set	MMT-430A, MMT-431A, MMT-432A, MMT-433A, MMT-440A, MMT-441A, MMT-442A, MMT-443A
MiniMed reservoir	MMT-332A
Medtronic Extended reservoir	MMT-342
Optional Devices	**Model Numbers**
MiniMed Mobile Application (Android)	MMT-6101
MiniMed Mobile Application (iOS)	MMT-6102
CareLink Connect Application (Android)	MMT-6111
CareLink Connect Application (iOS)	MMT-6112
Blue Adapter	ACC-190
CareLink Online (Personal)	MMT-7333
CareLink Pro	MMT-7335
Medtronic Diabetes Updates Application (Android)	MMT-6121
Medtronic Diabetes Updates Application (iOS)	MMT-6122

This medical device product has functions subject to FDA premarket review as well as functions (e.g., the MiniMed Mobile Applications) that are not subject to FDA premarket review. For this application, if the product has functions that are not subject to FDA premarket review, FDA assessed those functions only to the extent that they either could adversely impact the safety and effectiveness of the functions subject to FDA premarket review or they are included as a labeled positive impact that was considered in the assessment of the functions subject to FDA premarket review.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the management of diabetes, including a combination of various therapeutic and behavioral methods.

Self-behaviors including healthy eating, taking the clinically indicated medications (pharmaco-vigilance), and being physically active are fundamental lifestyle activities that are important for achieving glycemic control regardless of the methods of monitoring glucose and insulin administration.

Methods of monitoring glycemic control include periodic measurement of Hemoglobin A1c (HbA1c) which reflects mean blood levels control over a three-month period. This test is ordered and interpreted by the person with diabetes (PWDs) healthcare provider. Self-monitoring of blood glucose using glucose meters and test strips provides quantitative measurements of blood glucose at a single point in time for PWDs and their

healthcare providers. This helps to monitor the effectiveness of glycemic control, as well as in making more immediate treatment modifications.

An insulin pump is an alternative to multiple daily insulin injections (via insulin syringe or an insulin pen). PWDs may administer insulin by injection or using other insulin infusion pumps. There are currently several commercially available ambulatory insulin infusion pumps that can be used for insulin infusion. Additionally, sensor-augmented insulin infusion pumps or continuous glucose monitoring systems may be used to record continuous interstitial glucose information and provide real-time alerts for low and high glucose. Several available insulin pump systems offer automated features where insulin delivery may be suspended when sensor glucose has reached or is predicted to reach a user selected low glucose threshold. Hybrid closed loop insulin pump systems are also available for people with type 1 diabetes. These systems can automatically increase or decrease the amount of insulin delivered to maintain glucose within an optimal range.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The MiniMed 780G system has been commercially available in Europe since October 2020.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential device-related serious adverse events include

- Diabetic ketoacidosis (DKA) resulting from high blood glucose due to suspension of insulin delivery or inadequate insulin delivery (which may result from catheter occlusion, hardware or software malfunction, erroneous CGM readings in Auto Mode or suspend mode, or inadequate insulin dosing).
- Severe hypoglycemia resulting from over-delivery of insulin (which can result from hardware or software malfunction, erroneous CGM readings in Auto Mode, or erroneous insulin dosing), which may lead to seizure, unconsciousness and, rarely, death.

Potential device related non-serious events include:

- Skin irritation or redness
- Infection
- Pain or discomfort
- Bruising
- Edema
- Rash
- Bleeding
- Induration of skin
- Allergic reaction to adhesive

Sensor breakage with fragments retained under the skin is a potential adverse event related to use of the CGM component of the 780G system, but this was not observed during the clinical studies. Based on post-market experience with similar devices and the results observed in the clinical studies described below, the occurrence and severity of these events are low.

Infection at the insulin pump infusion set insertion site and sensor insertion site is a potential complication related to insertion of the CGM or the insulin pump infusion set. Based on post-market experience with similar devices, and the results observed in clinical studies, the occurrence and severity of these events are not expected to differ from other approved infusion sets and CGM devices.

Insulin pump use is known to carry an increased risk of DKA. However, FDA has received information indicating some patients are willing to accept an increased risk of DKA or ketosis and hyperglycemia (severe hyperglycemia) because of the benefits of pump use (see also Section XII below).

Like other insulin pumps, there is an inherent risk that users of the device who do not use the 780G system as intended could harm themselves. Therefore, the device is for prescription use only and contraindicated for people unwilling or unable to perform fingerstick blood glucose meter readings and for people unwilling or unable to maintain contact with their healthcare professional.

As demonstrated under P120010/S046 for the MiniMed 530G system (which has the same 'suspend on low' feature, where insulin delivery will suspend for two hours after the low glucose threshold has been reached), two-hour suspension of insulin delivery is unlikely to lead to clinically significant ketosis or ketoacidosis even if the pump inappropriately suspends when blood sugar is normal or elevated and should respond to insulin therapy and hydration within a few hours.

There is a theoretical risk of insulin over-delivery due to device malfunction which has a risk of leading to severe hypoglycemia due to malfunction of the 780G system. However, this event did not occur during the pivotal study or the continuation phase of the pivotal study. If insulin over-delivery were to occur, there are several mechanisms in place, designed to help detect and mitigate the risk of impending and/or current hypoglycemia, including the presence of alarms/alerts and insulin delivery suspension/reduction.

There is a theoretical risk of insulin under-delivery (due to a hardware or software malfunction) which may lead to severe hyperglycemia or DKA due to malfunction of the 780G system. However, this event did not occur during the pivotal study or the continuation phase of the pivotal study. If insulin under-delivery were to occur, there are mechanisms in place to help detect impending and/or current hyperglycemia, including the presence of alerts and alarms.

The consequences of falsely high glucose readings on the CGM would be potential over-delivery of insulin via automated insulin delivery and missed low glucose suspensions and alerts/alarms, which have the potential to lead to severe hypoglycemia.

The consequences of falsely low glucose readings on the continuous glucose monitor would be potential under-delivery of insulin and missed high glucose alerts, which have the potential to lead to severe hyperglycemia or DKA.

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Pre-clinical testing of the MiniMed 770G pump hardware supports the safe use of the 780G pump as these pumps contain identical hardware. Please see the SSED for P160017/S076 for descriptions of pre-clinical testing of the pump hardware.

The Guardian Sensor (3) and One-Press Serter remain unchanged. Please see the SSED for P160017 for descriptions of the pre-clinical testing of the Guardian Sensor (3) and One- Press Serter.

The Guardian Link (3) Transmitter and Accu-Chek Guide™ Link Meter remain unchanged since their approval under P160017/S076. Please see the SSED for P160017/S076 for descriptions of the pre-clinical testing of the Guardian Link (3) Transmitter and Accu-Chek Guide™ Link Meter.

The Guardian 4 sensor is physically the same device as the Guardian Sensor (3) approved under PMA P160017. Therefore, the pre-clinical testing that was approved for the Guardian Sensor (3) under PMA P160017 also applies to Guardian 4 sensor. Please see the SSED for P160017 for descriptions of the pre-clinical testing of the Sensor.

The Guardian 4 transmitter shares the same mechanical and electrical hardware as the Guardian Link (3) transmitter (MMT-7911) (GST5C) approved under P160017/S076. Requirements related to hardware only or hardware interface only features are hence not impacted, and GST5C verification data that was approved under P160017/S076 is applicable to the Guardian 4 transmitter. Please see the SSED for P160017/076 for descriptions of the pre-clinical testing of the transmitter.

Testing was conducted to evaluate the software impact on the transmitter battery. Results confirmed that the battery met all requirements, demonstrating that the software had no effects on transmitter battery performance. Table 3 provides details of the requirements and acceptance criteria.

Table 3: Guardian 4 Transmitter (MMT-7841) Battery Life Testing

Test	Sample Size	Requirement	Acceptance Criteria	Results
Battery Life	29	GST-PS-345: The GST shall store data for at least the life of the sensor.	The testing must demonstrate that the product stores data for at least the life of the sensor.	Pass
		GST-PS-432: Under normal use, a fully charged GST battery shall operate the device for the duration of 1 sensor use.	The testing must demonstrate that, under normal use and starting at full charge, the product's battery shall operate the device for the duration of 1 sensor use.	
		GST-PS-160: The GST shall transmit an alert at the detection of a depleted battery condition.	The testing must demonstrate that the product transmits an alert at the detection of a depleted battery condition.	
		GST-PS-161: The GST shall transmit an alert at the detection of a low battery condition.	The testing must demonstrate that the product transmits an alert at the detection of a low battery condition.	
		GST-PS-164: The time from the low battery alert to the depleted battery alert shall be at least 1 day under normal use.	The testing must demonstrate that the time from the low battery alert to the depleted battery alert is at least 1 day under normal use.	
		GST-HRS-210: The memory shall store data for at least the life of the sensor per sensor life.	The testing must demonstrate that the memory shall store data for at least the life of the sensor per sensor life.	
		GST-HRS-203: A fully charged GST battery shall operate the device for at least the life of the sensor.	The testing must demonstrate that, starting at full charge, the product battery shall operate the device for at least the life of the sensor.	

MiniMed 780G System

System testing of the MiniMed 770G system supports the safe use of the 780G system as the system hardware components (i.e., pump, transmitters, and blood glucose meter) remain unchanged since their approval as part of the 770G system under P160017/S076. Application-level verifications were performed on the full MiniMed 780G system (i.e. MiniMed 780G pump, transmitters, BG meter, MiniMed Mobile App, CareLink, and CareLink Connect App) to ensure that the devices are

compatible, and that data is successfully transferred. Please see the SSED for P160017/S076 for all other system testing.

Packaging

Pre-clinical testing performed on the MiniMed 770G pump hardware and packaging supports the 780G pump as the corresponding pump hardware and packaging are identical. Please see the SSED for P160017/S076 for packaging validation.

Please see the SSED for P160017 for descriptions of the pre-clinical packaging validation conducted for the Guardian Link (3) Transmitter and Guardian Sensor (3) and Guardian 4 Transmitter and Guardian 4 Sensor.

Software

Comprehensive verification and validation testing were conducted to confirm that the software used in the MiniMed 780G system meets all specified requirements and that the software will operate reliably and safely under normal or abnormal use conditions.

Software verification and validation were conducted in accordance with the FDA Guidance Document entitled *General Principles of Software Validation: Final Guidance for Industry and FDA Staff (issued on January 11, 2002)*. Software development activities included establishing detailed software requirements, linking requirements with associate verification tests, software code reviews, unit testing, system level testing and defect tracking and dispositioning to ensure the software conforms to user needs and intended uses.

Firmware Over the Air (FOTA)

The MiniMed 780G pump has the capability to securely receive and install firmware-over-the-air (FOTA) updates, via the FOTA app. Verification of the FOTA functionality in the MiniMed 770G pump software, which supports safe use of the FOTA feature, is applicable to the 780G pump as the FOTA architecture and components are identical for both pumps.

Human Factors Testing

Human Factors usability validation studies were conducted in alignment with the IEC 62366-1 standard entitled *Medical Devices – Application of Usability Engineering to Medical Devices* and the FDA Guidance Document entitled *Applying Human Factors and Usability Engineering to Medical Device*.

The applicant conducted usability validation studies to evaluate use of the MiniMed 780G system by patients with type 1 diabetes mellitus ages 7 years and older. These studies address use of the 780G system with compatible CGMs: Guardian 3 Sensor / Guardian Link 3 Transmitter and Guardian 4 sensor / Guardian 4 transmitter.

For use of the 780G system with the Guardian 3 CGM, Medtronic conducted two

usability studies. In the first usability study, users representing both adult and pediatric pump users (some with a caregiver) with varying levels of pump experience performed critical tasks associated with using the MiniMed 780G system in both Manual and Auto Modes. Task Analyses were conducted to determine 780G system critical tasks. Representative user groups were identified as follows:

- Novice Insulin Pump Users (pediatric and adult).
  Users in these groups were new to insulin pump and used injections, shots or insulin pens only.
- Experienced Insulin Pump Users (pediatric and adult).
  Users in these groups were using any insulin pump except 670G.
- Current 670G Insulin Pump Users (pediatric and adult).
  Users in these groups were using the 670G Insulin Pump at the time and were on Auto Mode for at least 1 month.

In a supplementary usability study, users representing only novice adult and pediatric pump users (some with a caregiver) performed critical tasks associated with using the 780G system in both Manual and Auto modes. Representative users were new to insulin pumps and CGM and used injections, shots or insulin pens only. For use of the 780G system with the Guardian 4 CGM, a human factors assessment was performed to evaluate usability risks as compared to use of the 780G system with the Guardian 3 CGM (assessed as described above). All workflow and potential use errors for Guardian Sensor (3) and Guardian 4 sensor were found to be equivalent when used adjunctively. Thus, the results of human factor validation studies for the Guardian 3 CGM are applicable to the Guardian 4 CGM.

For all the usability studies conducted, all use errors, close calls and use difficulties observed during completion of critical tasks were analyzed, and the root causes and impacts were assessed. For any use errors and close calls, a residual risk analysis was performed to: (a) determine whether design changes would further reduce the risks, and (b) assess the residual risks in relation to the benefits to the patient. It was determined that no design changes were necessary. Overall, the human factors usability validation studies and assessment demonstrated that the MiniMed 780G system, used with either the Guardian 3 CGM or the Guardian 4 CGM, is safe and effective for use by patients ages 7 years and older with type 1 diabetes.

B. Animal Studies

None

C. Additional Studies

None

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

A pivotal clinical study was performed using the MiniMed 670G 4.0 insulin pump, which contains the same Advanced Hybrid Closed Loop (AHCL) algorithm as the

MiniMed 780G insulin pump, the Guardian Sensor (3) and the Guardian Link (3) Transmitter. The applicant also conducted a clinical study of the Guardian 4 sensor with the Guardian 4 transmitter.
A brief summary of the supporting clinical studies is presented below in Table 4.

Table 4: Summary of P160017/S091 Clinical Studies

Clinical Study	Patient Population	Study Design/Objective
Safety Evaluation of the Advanced Hybrid Closed Loop (AHCL) System in Type 1 Adult and Pediatric Subjects.	7-75 years	Multi-center, single arm study in insulin-requiring adult and pediatric subjects with type 1 diabetes. The objective of the study is to collect in-home data using the AHCL system.
Performance Evaluation of an Advanced Algorithm with CGM in Adults, Adolescents, and Pediatrics	7-80 years	Multi-center, randomly assigned, prospective, single-sample correlational design without controls. The primary objective of the study is to demonstrate the accuracy of G4S when used over a period of 7 days (i.e., 170 hours) with the system in subjects 2-80 years of age.

Pivotal Study: Safety Evaluation of the Advanced Hybrid Closed Loop (AHCL) System in Type 1 Adult and Pediatric Subjects:

A. Study Design

The study was a multi-center, single-arm study for adult and pediatric subjects with type 1 diabetes in a home setting. Subjects were treated between June 7, 2019 and March 17, 2021.

A total of 329 subjects aged 7–75 years with type 1 diabetes were enrolled at 19 investigational sites across the United States, and 275 of those subjects completed the study period. Of the 275 subjects who completed the study, 151 were age 7-17 years and 124 were age 18 and older (see subject accountability below).

Subjects who completed the study period wore the MiniMed 670G 4.0 pump with the Guardian Link (3) Transmitter, the Guardian Sensor (3) and infusion sets for approximately 4-5 months and participated in all study phases: a two-week run-in

period and 90-day at-home use period. Subjects were instructed to use the device in Auto Mode for the duration of the 90-day at-home study.

Run-in period

The run-in period allowed subjects to become familiar with the new study devices. During this period, subjects used the Study Pump (MiniMed 670G 4.0) without activating the auto correction feature.

Subjects were asked to complete a Regular Sized Dinner Challenge with Missed Meal Bolus, in which the subject consumed dinner without administering a Meal Bolus. Subjects were asked to check BG at the start of the meal, as well as 2 hours and 4 hours after the meal, and provide correction boluses as necessary.

Study Period

All subjects continued using the Study Pump and began to use the pump in Auto Mode for 90 days during the study period. Subjects were expected to use the pump in Auto Mode for the entire study period. If subjects were kicked out of Auto Mode, they were expected to try to mitigate the issue and return to Auto Mode as soon as possible. Per investigator discretion, subjects' target basal setpoint was set at either 100 mg/dL or 120 mg/dL to start the study period and the setpoint was changed after 45 days (± 5 days) of the study period. For example: a subject who started the study period with the 100 mg/dL setpoint underwent a change to the 120 mg/dL setpoint after 45 days. Subjects were also asked to complete a series of meal and exercise challenges during this period.

1. Clinical Inclusion and Exclusion Criteria

   Subjects were considered for enrollment in the study if they met all of the following criteria:

   General Inclusion Criteria

   1. Subject is age 7–75 years at time of screening
   2. Subjects 14–75 years of age: A clinical diagnosis of type 1 diabetes for 2 years or more as determined via medical record or source documentation by an individual qualified to make a medical diagnosis
   3. Subjects 7-13 years of age: A clinical diagnosis of type 1 diabetes for 1 year or more as determined via medical record or source documentation by an individual qualified to make a medical diagnosis

   Study-Specific Inclusion Criteria

   4. Subject is willing to perform ≥ 4 finger stick blood glucose measurements daily
   5. Subject is willing to perform required sensor calibrations
   6. Subject is willing to wear the system continuously throughout the study
   7. Subject must have a minimum daily insulin requirement (Total Daily

Dose) of greater than or equal to 8 units

8. Subject has a Glycosylated hemoglobin (HbA1c) less than 10%(as processed by Central Lab) at time of Screening visit
   Note: All HbA1c blood specimens will be sent to and tested by a NGSP certified Central Laboratory. HbA1c testing must follow National Glycohemoglobin Standardization Program (NGSP) standards.
9. Subject has TSH in the normal range OR if the TSH is out of normal reference range the Free T3 is below or within the lab's reference range and Free T4 is within the normal reference range.
10. Pump therapy for greater than 6 months prior to screening (with or without CGM experience)
11. Subject must have a companion or caregiver available at night for the duration of the study period who resides (or will live) in the same building (or home). A companion or caregiver should also be available during exercise challenges in the same building, home or location (if not at home). This requirement may be verified by subject report at screening visit.
12. Subject willing to upload data from the study pump, must have Internet access and a computer system that meets the requirements for uploading the study pump
13. If subject has celiac disease, it has been adequately treated as determined by the investigator
14. Subject is willing to take one of the following insulins and can financially support the use of either of the 2 insulin preparations throughout the course of the study (i.e., co-payments for insulin with insurance or able to pay full amount)
    - Humalog™* (insulin lispro injection)
    - NovoLog™* (insulin aspart)
15. Subjects with history of cardiovascular event 1 year or more from the time of screening must have an EKG within 6 months prior to screening or during screening. If subject has an abnormal EKG, participation is allowed if there is clearance from a cardiologist
16. Subjects with 3 or more of the cardiovascular risk factors listed below must have an EKG within 6 months prior to screening or during screening. If subject has an abnormal EKG, participation is allowed if there is clearance from a cardiologist
    a. Cardiovascular risk factors include:
       - Age >35 years
       - Type 1 diabetes of >15 years' duration
       - Presence of any additional risk factor for coronary artery disease
       - Presence of microvascular disease (proliferative retinopathy or nephropathy, including microalbuminuria)
       - Presence of peripheral vascular disease
       - Presence of autonomic neuropathy

Subjects with history of cardiovascular event 1 year or more from the time of screening must have a stress test within 6 months prior to screening or during run

in period. If subject fails stress test, participation is allowed if there is clearance from a cardiologist

Subjects were not permitted to enroll in the pivotal study if they met any of the following criteria:

Exclusion Criteria

1. Subject has a history of 1 or more episodes of severe hypoglycemia, which resulted in any the following during the 6 months prior to Screening:
    a. Medical assistance (i.e., Paramedics, Emergency Room (ER) or Hospitalization)
    b. Coma
    c. Seizures
2. Subject has been hospitalized or has visited the ER in the 6 months prior to Screening resulting in a primary diagnosis of uncontrolled diabetes
3. Subject has had Diabetic Ketoacidosis (DKA) in the 6 months prior to Screening.
4. Subject has Hypoglycemia Unawareness, measured by the Gold questionnaire as ≥ 4 (Gold, Macleod et al. 1994) at Screening
5. Subject is unable to tolerate tape adhesive in the area of sensor placement
6. Subject has any unresolved adverse skin condition in the area of sensor placement (e.g., psoriasis, dermatitis herpetiformis, rash, Staphylococcus infection)
7. Women of child-bearing potential who have a positive pregnancy test at Screening or plan to become pregnant during the course of the study
8. Females who are sexually active and able to conceive will be excluded if they are not using an effective method of contraception and do not agree to continue using an effective method of contraception for the duration of the study as determined by investigator.
9. Subject has had any of the following cardiovascular events within 1 year of screening: myocardial infarction, unstable angina, coronary artery bypass surgery, coronary artery stenting, transient ischemic attack, cerebrovascular accident, angina, congestive heart failure, ventricular rhythm disturbances or thromboembolic disease
10. Subject is being treated for hyperthyroidism at time of Screening
11. Subject has a diagnosis of adrenal insufficiency
12. Subject has taken any oral, injectable, or intravenous (IV) glucocorticoids within 8 weeks from time of Screening, or plans to take any oral, injectable, or IV glucocorticoids during the course of the study
13. Subject is actively participating in an investigational study (drug or device) wherein he/she has received treatment from an investigational study drug or investigational study device in the last 2 weeks
14. Subject is currently abusing illicit drugs
15. Subject is currently abusing marijuana
16. Subject is currently abusing prescription drugs
17. Subject is currently abusing alcohol

18. Subject is using pramlintide (Symlin), DPP-4 inhibitor, liraglutide (Victoza or other GLP-1 agonists), metformin, canagliflozin (Invokana or other SGLT2 inhibitors) at time of Screening
19. Subject has a history of visual impairment which would not allow subject to participate in the study and perform all study procedures safely, as determined by the investigator
20. Subject has elective surgery planned that requires general anesthesia during the course of the study
21. Subject has a sickle cell disease, hemoglobinopathy; or has received red blood cell transfusion or erythropoietin within 3 months prior to time of Screening
22. Subject plans to receive red blood cell transfusion or erythropoietin over the course of study participation
23. Subject diagnosed with current eating disorder such as anorexia or bulimia
24. Subject has been diagnosed with chronic kidney disease that results in chronic anemia
25. Subject has a hematocrit that is below the normal reference range of lab used.
26. Subject is on dialysis
27. Subject has serum creatinine of >2 mg/dL.
28. Research staff involved with the study.

2. Follow-up Schedule

There were four scheduled office visits throughout the run-in period. During the first visit, subjects were screened for eligibility and were asked to complete questionnaires about their experience with their currently used device and had blood collected for an HbA1c test. The remaining visits were meant to allow the subjects to familiarize themselves with the study devices.

Throughout the study period there were a number of scheduled visits (telephone calls and office visits). These visits were meant to ensure that the subject was healthy and to remind them to adhere to the study requirements, for example, reminders to only insert glucose sensors in locations that are specified in the User Guide materials.

During the final visit, subjects were asked to complete some questionnaires about their experience and also had blood collected for an HbA1c test.

3. Clinical Endpoints

There were no statistically powered endpoints in the pivotal study, nor was there any hypothesis testing. This was a descriptive study to evaluate the safe use of the AHCL system.

Descriptive Endpoints

- The mean change in HbA1c will be presented from baseline to end of study

period
- Change of Total Daily Dose (TDD) of insulin from baseline to end of study period
- Change of weight from baseline to end of study period
- Time spent in Auto Mode versus time spend in Manual Mode
- Time in different range (% of SG): SG < 50, 54, 60, 70 mg/dL, SG > 140, 180, 250, 350 mg/dL
- Number of Events, Area Under Curve (AUC) and Time in the hyperglycemic range: sensor glucose (SG) > 140, 180, 250, 350 mg/dL
- Number of Events, AUC and Time in the hypoglycemic range: SG < 50, 54, 60, and 70 mg/dL
    - Change in BG values during meal challenge (BG prior and BG 2 hours after meal)
    - Change in % of time in euglycemia (70-180 mg/dL) during meal challenge, prior and 2 hours after meal
    - Difference in AUC during meal challenge prior and 2 hours after meal
- Analysis will be performed for
    - Age
        - 7 – 13
        - 14 – 75
    - Setpoint
        - 100 mg/dL
        - 120 mg/dL
    - Temp Target usage
        - Yes
        - No

Safety Data Summarized
- Serious Adverse Event (SAE)
- Serious Adverse Device Effects (SADE)
- Unanticipated Adverse Device Effect (UADE)
- Incidence of Severe Hypoglycemia
- Incidence of DKA

B. Accountability of PMA Cohort

A total of 299 subjects entered the run-in period, 10 subjects withdrew during the run-in period and 289 entered the study period: 161 subjects aged 7-17 years and 128 subjects aged 18-75 years. Ten (10) subjects aged 7-17 years and four (4) subjects aged 18-75 years withdrew during the study period. Therefore, a total of 275 subjects completed the study period: 151 subjects aged 7-17 years and 124 subjects aged 18-75 years.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population as listed in Table 5 are typical for studies performed in the Type 1 diabetes population in the US.

Table 5: Study Demographics

Characteristic	Subjects 7-17-years-old Number of Subjects = 160*	Subjects 18-75-years-old Number of Subjects = 128
Age (Years)		
n	160	128
Mean (SD)	11.3 (2.5)	43.5 (15.2)
Median	11.0	45.5
Min, Max	7.0, 17.0	18.0, 75.0
Gender N(%)		
Female	83 (51.9%)	69 (53.9%)
Male	77 (48.1%)	59 (46.1%)
Race N(%)		
White	144 (90.0%)	123 (96.1%)
Asian	3 (1.9%)	2 (1.6%)
American Indian or Alaska Native, White	1 (0.6%)	0 (0.0%)
Asian, White	3 (1.9%)	0 (0.0%)
Black/African American	4 (2.5%)	1 (0.8%)
Native Hawaiian or Other Pacific Islander	1 (0.6%)	0 (0.0%)
Other	4 (2.5%)	2 (1.6%)
Ethnicity N(%)		
Hispanic Or Latino	12 (7.5%)	7 (5.5%)
Not Hispanic Or Latino	148 (92.5%)	120 (93.8%)
Not Reported	0 (0.0%)	1 (0.8%)
Diabetes History (Years)		
n	160	128
Mean (SD)	6.2 (2.9)	25.8 (12.7)
Median	5.8	23.7
Min, Max	1.1, 15.0	3.9, 60.7
Height (cm)		
n	160	128
Mean (SD)	150.5 (15.4)	171.0 (9.4)
Median	151.2	170.1
Min, Max	116.2, 200.6	152.9, 195.0
Weight (kg)		
n	160	128
Mean (SD)	45.8 (14.8)	83.3 (18.5)
Median	43.1	80.2
Min, Max	21.4, 91.9	57.7, 165.9

Characteristic	Subjects 7-17-years-old Number of Subjects = 160*	Subjects 18-75-years-old Number of Subjects = 128
BMI (Kg/m2)		
n	160	128
Mean (SD)	19.7 (3.5)	28.4 (5.6)
Median	18.8	27.1
Min, Max	14.1, 33.4	18.3, 51.2
Baseline A1C (%)		
n	160	128
Mean (SD)	7.9 (0.9)	7.4 (0.8)
Median	7.9	7.5
Min, Max	6.1, 9.9	5.7, 9.8

*Although 161 subjects entered the Study Period, one subject exited the Study Period without using Auto Mode

D. Safety and Effectiveness Results

1. Safety Results

The safety of the device was assessed by evaluating the incidence of all serious Adverse Events (AEs), Adverse Device Events (ADEs), Serious Adverse Device Events (SADEs), and Unanticipated Adverse Device Effects (UADEs) experienced by study subjects. AEs were listed in terms of severity and relationship to the device.

Subjects 7-17 Years of Age:

There were two (2) reports of serious adverse events:

- One (1) event was an incident of severe hypoglycemia during the run-in period. This event was determined to be neither device nor procedure related but was considered serious due to reported seizure. The subject recovered after receiving a 1 mg dose of glucagon and eating peanut butter and more carbs. There were no subsequent lows. The subject was in manual mode at the time of the event and did not treat or respond to low alerts prior to the severe hypoglycemia event.
- Another event was presented to the emergency department (ED) with abdominal pain during the study period. BG was 113 mg/dL and ketones were 0.4. Subject was administered IV fluids and 4 mg oral ondansetron. Subject turned off Auto Mode but remained on pump and was admitted to hospital for overnight observation. Subject was discharged the next day with symptoms resolved. DKA ruled out, primary diagnoses were dehydration and constipation. This event was determined to be neither device nor procedure related and was resolved without infusion set change.

There were no reports of unanticipated serious adverse device effects.

There were no reports of unanticipated non-serious adverse device/procedure effects.

There were no reports of diabetic ketoacidosis events,

There were 39 severe hyperglycemia events reported.

Severe hyperglycemia was defined in the protocol as a glucose concentration >300 mg/dL (or 16.7 mmol/L) with blood glucose ketones greater than (>) 1.5 mmol/L, urine ketones moderate or large, or accompanied by symptoms of nausea, vomiting or abdominal pain.

Of the 39 reported severe hyperglycemia events, 22 were thought to be device-related. The 22 device-related severe hyperglycemia events were believed to be due to infusion set issues (i.e., occlusion, bent cannula or cannula pull out).

Subjects 18-75 Years of Age:
There were two reports of serious adverse events. These events were an incident of appendicitis and an incident of sepsis secondary to pyelonephritis and were not related to the study device.

There were no reports of unanticipated serious adverse device effects.

There were no reports of unanticipated non-serious adverse device/procedure effects.

There were no reports of diabetic ketoacidosis events.

There were no reports of severe hypoglycemia events.

There were 4 severe hyperglycemia events reported. Of the 4 reported severe hyperglycemia events, 3 were thought to be device-related. The 3 device-related severe hyperglycemia events were believed to be due to infusion set issues (i.e., occlusion, bent cannula or cannula pull out).

Adverse effects that occurred in the PMA clinical study:

There were no reports of unanticipated serious adverse device effects.
There were no reports of unanticipated non-serious adverse device/procedural effects.
There were no reports of diabetic ketoacidosis events.
There was one event of severe hypoglycemia reported.

2. Effectiveness Results

The data below describes how the device performed during the AHCL pivotal study. This study compared the results of subjects prior to using the auto correction bolus (run-in period - 2 weeks) against results while using the auto correction bolus (study period - 3 months). However, the study did not evaluate subjects who were not using a system equipped with the auto correction bolus

(i.e., there was no control group).

Table 6 below provides an overall summary of the run-in period and study period for all subjects with Auto Mode enabled in the study period. Table 7 and Table 8 provide mean sensor glucose values in specific glucose ranges during run-in, day 1, and study period. The data below suggest that adult subjects spent more time in range (70–180 mg/dL), less time in hypoglycemia (<70 mg/dL) and less time in hyperglycemia (>180 mg/dL) during the study period compared with the run-in period. Pediatric subjects spent more time in range (70-180 mg/dL and less time in hyperglycemia (>180 mg/dL) without increasing time in hypoglycemia (<70 mg/dL) during the study period compared with the run-in period.

Table 6: Mean Sensor Glucose during Run-in and Study Period with 780G/GS3

Parameter	Age 7-17 Years (n=160)		Age 18-75 Years (n=128)	
	Run-In	Study	Run-In	Study
Sensor Glucose, (mg/dL) Mean (SD), (95% CI)	168.8 (19.9), (165.7, 171.9)	152.7 (10.6), (151.0, 154.3)	151.1 (15.1), (148.5, 153.8)	147.4 (10.7), (145.5, 149.3)

Table 7: Mean Percent Sensor Glucose Values in Specific Glucose Ranges (Mean ± SD) with 780G/GS3 for Day 1, Run-in, and Study Period

Glucose Range (mg/dL)	Age 7-17 Years (n=160)			Age 18-75 Years (n=128)		
	Run-In	Study Period (Day 1)	Study Period (Overall)	Run-In	Study Period (Day 1)	Study Period (Overall)
< 50	0.4 ± 0.5	0.5 ± 0.6	0.4 ± 0.4	0.5 ± 0.7	0.4 ± 0.6	0.3 ± 0.4
< 54	0.7 ± 0.7	0.7 ± 0.7	0.6 ± 0.5	0.8 ± 1.1	0.7 ± 0.8	0.5 ± 0.6
< 60	1.2 ± 1.1	1.3 ± 1.1	1.2 ± 0.8	1.4 ± 1.7	1.2 ± 1.2	1.0 ± 0.9
< 70	2.7 ± 2.0	3.0 ± 1.8	2.7 ± 1.6	3.4 ± 3.0	2.8 ± 2.2	2.3 ± 1.7
70–180	59.4 ± 11.8	67.9 ± 8.4	70.3 ± 6.5	70.5 ± 9.8	73.5 ± 8.8	75.0 ± 7.2
> 180	38.0 ± 12.4	29.2 ± 8.4	27.0 ± 6.7	26.2 ± 10.2	23.7 ± 9.0	22.6 ± 7.4
> 250	12.1 ± 7.5	8.5 ± 4.9	7.1 ± 3.8	5.5 ± 4.1	5.1 ± 4.2	4.4 ± 3.0
> 350	1.3 ± 1.6	0.8 ± 1.0	0.7 ± 0.8	0.4 ± 0.6	0.4 ± 0.7	0.3 ± 0.4

The pivotal study included a continued access phase whereby subjects transitioned from the MiniMed 670G 4.0 system to the MiniMed 780G system with Guardian 4 Sensor and Guardian 4 transmitter. The study results are comparable for the MiniMed 780G system. Table 8 provides the mean sensor glucose values in specific glucose ranges for 780G system with the Guardian 4 CGM for Day 1 and the study period.

Table 8: Mean Percent Sensor Glucose Values in Specific Glucose Ranges (Mean ± SD) with 780G/GS4 for Day 1 and Study Period

Glucose Range (mg/dL)	Age 7-17 Years (n=160)		Age 18-75 Years (n=128)	
	Study Period (Day 1)	Study Period (Overall)	Study Period (Day 1)	Study Period (Overall)
< 50	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
< 54	0.5 ± 0.6	0.4 ± 0.4	0.4 ± 0.4	0.3 ± 0.3
< 60	1.0 ± 0.9	0.8 ± 0.7	0.7 ± 0.7	0.5 ± 0.5
< 70	2.3 ± 1.6	2.2 ± 1.4	1.9 ± 1.4	1.6 ± 1.1
70–180	67.3 ± 9.8	71.5 ± 7.8	72.6 ± 10.8	76.6 ± 9.0
> 180	30.4 ± 10.0	26.3 ± 8.1	25.5 ± 11.0	21.8 ± 9.3
> 250	9.2 ± 6.3	6.9 ± 4.5	5.7 ± 5.5	4.2 ± 3.8
> 350	1.2 ± 2.0	0.7 ± 1.1	0.4 ± 1.0	0.3 ± 0.5

Each subject's baseline HbA1c value was collected at enrollment. The end-of-study HbA1c was collected at the last visit of the study period. The mean change in HbA1c from the first visit and last visit was analyzed and found to be -0.5% for both subject groups, 7-17 years of age and 18-75 years of age (with 95% confidence intervals of -0.6 to -0.4). A summary of HbA1c data is provided in Table 9 below.

Table 9: Percent Change in HbA1c from Baseline to End of Study

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	Baseline (SD)	End of Study (SD)	Change from Baseline to End of Study (SD)	Baseline (SD)	End of Study (SD)	Change from Baseline to End of Study (SD)
Number of Subjects	160	136	136	128	127	127
HbA1c, %, Mean (SD)	7.9 (0.9)	7.4 (0.7)	-0.5 (0.7)	7.4 (0.8)	6.9 (0.5)	-0.5 (0.6)
HbA1c, %, Median	7.9	7.3	-0.5	7.5	7	-0.4
95% Confidence Interval	(7.8, 8.0)	(7.3, 7.5)	(-0.6, -0.4)	(7.3, 7.6)	(6.9, 7.0)	(-0.6, -0.4)

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	Baseline (SD)	End of Study (SD)	Change from Baseline to End of Study (SD)	Baseline (SD)	End of Study (SD)	Change from Baseline to End of Study (SD)
HbA1c, %, Min, Max	6.1, 9.9	6.2, 9.1	-2.7, 1.7	5.7, 9.8	5.9, 8.6	-2.8, 0.7

Table 10 below summarizes time spent in Auto Mode and sensor usage from the start of the study period until the end of the study period. This data shows that subjects were in Auto Mode for greater than 90% of the time.

Table 10: Summary of Sensor Usage and Time Spent in Auto Mode, From Start of Auto-Mode to End of the Study Period

Category	Percentage of Time	
	Subject 7-17 Years of Age	Subject 18-75 Years of Age
Time spent using sensor	88.0%	91.2%
Time spent not using sensor	12.0%	8.8%
Time spent in Auto Mode	93.5%	95.2%
Time spent in Manual Mode	6.5%	4.8%

During the study, subjects performed meal challenges which involved eating a meal without giving a meal bolus. These challenges were intended to evaluate how subjects' glucose would respond when a meal dose is occasionally missed. Missed meal boluses when in Auto Mode with the auto correction bolus enabled at the 100 mg/dL and 120 mg/dL SG setpoints were compared to missed meal boluses when in Manual mode. Table 11 below shows the mean SG values up to two hours before, and 1 to 3 hours after, a regular-sized dinner with a missed meal bolus during the run-in and study periods.

Although the goal is to spend more time in range (70-180 mg/dL), patients SG values may rise to the hyperglycemic range (>180 mg/dL) if they do not bolus when they eat.

Table 11: Mean SG values During Regular Sized Dinner with Missed Meal Bolus, Analysis for Data Collected During Run-In and Study Period

Category	Subject 7-17 Years of Age (N=94)			Subject 18-75 Years of Age (N=70)		
	Baseline	Study Period		Baseline	Study Period	
		Setpoint 100 mg/dL	Setpoint 120 mg/dL		Setpoint 100 mg/dL	Setpoint 120 mg/dL
Mean SG before	140.6 ±	152.9 ±	151.5 ±	132.9 ±	138.0 ±	139.8 ±

Category	Subject 7-17 Years of Age (N=94)			Subject 18-75 Years of Age (N=70)		
	Baseline	Study Period		Baseline	Study Period	
		Setpoint 100 mg/ dL	Setpoint 120 mg/ dL		Setpoint 100 mg/ dL	Setpoint 120 mg/ dL
meal (mg/dL), Mean ± SD	48.0	50.5	43.6	42.3	51.5	38.7
Mean SG 2 Hours after meal (mg/dL), Mean ± SD	255.6 ± 65.0	204.7 ± 53.8	202.6 ± 51.4	210.5 ± 53.3	198.8 ± 53.3	203.1 ± 41.6
Change in Mean SG before and after the meal (mg/dL), Mean ± SD	115.0 ± 81.6	51.8 ± 62.3	51.0 ± 71.3	77.6 ± 68.5	60.8 ± 75.0	63.4 ± 60.7

During the study period, subjects exercised on 3 consecutive days while in Auto Mode with the auto correction bolus enabled at the 100 mg/dL and 120 mg/dL setpoints, with the Temp Target feature turned ON. Temp Target allows the user to temporarily change the SG setpoint to 150 mg/dL. When Temp Target is enabled, Auto Mode reverts to the previous SG setpoint after the user-set time at the 150 mg/dL setpoint elapses. Table 12 below shows the mean SG values up to two hours before, and 1 to 3 hours after, exercise during the study period only.

Table 12: Change in Mean SG values During Exercise

Category	Subject 7-17 Years of Age (N=131)		Subject 18-75 Years of Age (N=115)	
	Setpoint 100 mg/dL	Setpoint 120 mg/dL	Setpoint 100 mg/dL	Setpoint 120 mg/dL
Mean SG before exercise (mg/dL), Mean ± SD	154.6 ± 30.0	156.4 ± 34.8	141.6 ± 30.3	154.0 ± 30.9
Mean SG 2 Hour after exercise (mg/dL), Mean ± SD	149.9 ± 31.7	151.2 ± 33.4	134.1 ± 26.8	141.7 ± 31.4
Change in Mean SG before and after exercise (mg/dL), Mean ± SD	-4.7 ± 42.1	-5.2 ± 42.0	-7.5 ± 36.0	-12.3 ± 43.1

The two tables below, Table 13 and Table 14 show the results when subjects' pumps were programmed to setpoints of 100 mg/dL and 120 mg/dl, while also programmed to different active insulin times (AITs) according to the subjects' needs. These results show that subjects spent more time in range (70-180 mg/dL) from programming the setpoint to 100 mg/dL and the AIT to 2-3 hours.

Table 13: Glycemic Control Outcomes by Active Insulin Time, Setpoint 100 mg/dL, #*

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	AIT 120-180 minutes	**AIT 195-240 minutes**	**AIT>240 minutes**	**AIT 120-180 minutes**	**AIT 195-240 minutes**	**AIT>240 minutes**
Number of Subjects	107	52	2	74	54	4
Overall Average SG (mg/dL)	148.0 ± 11.8 (147.5)	153.1 ± 12.7 (151.2)	155.4 ± 9.1 (155.4)	141.4 ± 11.2 (141.0)	145.3 ± 10.4 (144.3)	145.1 ± 17.3 (150.8)
Overall SD SG (mg/dL)	56.7 ± 8.9 (56.1)	61.4 ± 8.7 (60.5)	61.6 ± 8.8 (61.6)	48.8 ± 7.9 (48.6)	51.8 ± 8.1 (50.8)	53.9 ± 7.8 (54.4)
Overall CV SG (%)	38.2 ± 4.3 (37.4)	40.0 ± 4.2 (39.6)	39.5 ± 3.3 (39.5)	34.4 ± 4.2 (34.3)	35.6 ± 4.6 (35.3)	37.1 ± 1.9 (36.3)
SG < 54 mg/dL (%)	0.7 ± 0.7 (0.5)	0.8 ± 0.8 (0.7)	0.3 ± 0.2 (0.3)	0.7 ± 0.8 (0.4)	0.6 ± 0.8 (0.3)	1.4 ± 1.1 (0.9)
SG < 70 mg/dL (%)	3.1 ± 2.0 (2.5)	3.5 ± 2.3 (3.0)	2.3 ± 0.5 (2.3)	2.9 ± 2.2 (2.4)	2.7 ± 2.2 (2.1)	4.8 ± 3.2 (3.7)
70-180 mg/dL (%)	71.9 ± 6.9 (72.0)	67.8 ± 6.8 (68.6)	68.0 ± 6.5 (68.0)	77.4 ± 7.4 (77.5)	74.8 ± 6.9 (75.7)	70.6 ± 7.9 (70.2)
SG > 180 mg/dL (%)	25.0 ± 7.1 (24.8)	28.7 ± 7.5 (27.8)	29.8 ± 6.0 (29.8)	19.7 ± 7.5 (19.2)	22.5 ± 6.9 (21.8)	24.6 ± 10.1 (26.6)
SG > 250 mg/dL (%)	6.3 ± 3.9 (5.5)	8.3 ± 4.3 (7.3)	8.6 ± 4.0 (8.6)	3.5 ± 2.8 (3.0)	4.5 ± 3.0 (4.0)	5.2 ± 3.5 (5.8)

*Values are presented by Mean ± SD (Median) except for number of subjects.
Subjects with at least 10 days' worth of CGM data in each AIT category and specific setpoint were included in analysis.

Table 14: Glycemic Control Outcomes by Active Insulin Time, Setpoint 120 mg/dL, #*

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	AIT 120-180 minutes	**AIT 195-240 minutes**	**AIT>240 minutes**	**AIT 120-180 minutes**	**AIT 195-240 minutes**	**AIT>240 minutes**
Number of Subjects	122	53	2	76	63	2
Overall Average SG (mg/dL)	153.8 ± 10.3 (153.6)	158.8 ± 11.7 (160.0)	166.9 ± 11.7 (166.9)	148.9 ± 10.8 (148.9)	153.5 ± 10.8 (153.0)	160.8 ± 16.3 (160.8)
Overall SD SG (mg/dL)	55.4 ± 9.0 (54.2)	58.5 ± 8.3 (58.9)	66.2 ± 3.3 (66.2)	47.5 ± 8.0 (46.7)	49.8 ± 8.6 (51.1)	57.0 ± 8.4 (57.0)
Overall CV SG (%)	35.9 ± 4.6 (36.1)	36.8 ± 4.0 (36.6)	39.7 ± 0.8 (39.7)	31.8 ± 4.0 (31.5)	32.4 ± 4.4 (33.1)	35.3 ± 1.6 (35.3)
SG < 54 mg/dL (%)	0.6 ± 0.6 (0.4)	0.6 ± 0.5 (0.4)	0.7 ± 0.7 (0.7)	0.4 ± 0.5 (0.3)	0.4 ± 0.5 (0.2)	0.3 ± 0.3 (0.3)

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes
SG < 70 mg/dL (%)	2.3 ± 1.6 (1.9)	2.2 ± 1.3 (2.0)	2.7 ± 2.0 (2.7)	2.0 ± 1.7 (1.6)	1.7 ± 1.3 (1.5)	1.4 ± 0.4 (1.4)
70-180 mg/dL (%)	71.1 ± 6.6 (70.9)	67.4 ± 7.6 (66.7)	60.6 ± 4.9 (60.6)	75.8 ± 7.2 (75.9)	72.5 ± 8.0 (72.4)	68.1 ± 10.7 (68.1)
SG > 180 mg/dL (%)	26.6 ± 6.8 (26.9)	30.4 ± 7.8 (31.0)	36.7 ± 7.0 (36.7)	22.2 ± 7.6 (21.6)	25.8 ± 8.2 (25.3)	30.5 ± 10.3 (30.5)
SG > 250 mg/dL (%)	6.7 ± 3.8 (5.8)	8.4 ± 4.1 (9.0)	13.2 ± 4.6 (13.2)	4.0 ± 3.0 (3.2)	5.1 ± 3.4 (4.6)	8.3 ± 4.8 (8.3)
*Values are presented by Mean ± SD (Median) except for number of subjects. # Subjects with at least 10 days' worth of CGM data in each AIT category and specific setpoint were included in analysis.						

Table 15 below provides the number of auto bolus events that occurred throughout the study period, glycemic control (i.e., average SG and percentage of SGs within various SG ranges) prior to and after auto bolus events, and the change in each category before and after auto bolus events. During the study period, 88,139 automatic correction boluses were administered for 7–17-year-old subjects and 68,962 automatic correction boluses were administered for 18–75-year-old subjects. The percentage of SGs in the hypoglycemic range (<70 mg/dL) did not increase for either subject population. The data below show that the auto correction bolus feature in the MiniMed 780G is safe.

*Table 15: Glycemic Control Prior to and After Auto Bolus Events, Study Period**

Category	Subject 7-17 Years of Age (N=160)			Subject 18-75 Years of Age (N=128)		
	2 hours prior event	6 hours post event	Change from Prior to Post	2 hours prior event	6 hours post event	Change from Prior to Post
Number of Auto Bolus Events	88139	88139	88139	68962	68962	68962
Sensor Glucose, Mean ± SD (95%CI)	158.8±10.0 (157.2, 160.4)	164.0±10.2 (162.4, 165.6)	5.2±2.8 (4.7, 5.6)	154.5±10.3 (152.7, 156.3)	159.1±10.1 (157.3, 160.8)	4.5±2.8 (4.0, 5.0)
SG < 50 mg/dL (%)	0.3±0.3 (0.3, 0.4)	0.3±0.3 (0.2, 0.3)	-0.1±0.1 (-0.1, -0.0)	0.3±0.3 (0.2, 0.3)	0.2±0.3 (0.2, 0.2)	-0.1±0.1 (-0.1, -0.0)
SG < 54 mg/dL (%)	0.5±0.4 (0.4, 0.6)	0.4±0.4 (0.4, 0.5)	-0.1±0.2 (-0.1, -0.1)	0.4±0.5 (0.3, 0.5)	0.3±0.4 (0.2, 0.4)	-0.1±0.2 (-0.1, -0.1)
SG < 60 mg/dL	0.9±0.7 (0.8, 1.1)	0.7±0.6 (0.6, 0.8)	-0.2±0.2 (-0.3, -0.2)	0.8±0.7 (0.6, 0.9)	0.6±0.6 (0.5, 0.7)	-0.2±0.3 (-0.2, -0.1)
SG < 70	2.2±1.3	1.6±1.0	-0.6±0.5	1.8±1.3	1.3±1.0	-0.5±0.5

Category	Subject 7-17 Years of Age (N=160)			Subject 18-75 Years of Age (N=128)		
	2 hours prior event	6 hours post event	Change from Prior to Post	2 hours prior event	6 hours post event	Change from Prior to Post
mg/dL (%)	(2.0, 2.4)	(1.4, 1.8)	(-0.7, -0.5)	(1.6, 2.0)	(1.1, 1.5)	(-0.6, -0.4)
70-140 mg/dL (%)	40.4±6.7 (39.4, 41.5)	37.3±6.2 (36.3, 38.3)	-3.1±2.0 (-3.4, -2.8)	40.8±8.7 (39.3, 42.3)	37.7±7.7 (36.3, 39.0)	-3.1±2.6 (-3.6, -2.7)
70-180 mg/dL (%)	68.8±7.4 (67.6, 70.0)	66.1±7.6 (64.9, 67.2)	-2.7±1.6 (-3.0, -2.5)	73.5±8.0 (72.1, 74.9)	71.2±8.3 (69.7, 72.6)	-2.3±1.5 (-2.6, -2.1)
SG >140 mg/dL (%)	57.4±7.2 (56.3, 58.5)	61.1±6.5 (60.1, 62.1)	3.7±2.3 (3.3, 4.0)	57.4±9.4 (55.8, 59.1)	61.0±8.1 (59.6, 62.4)	3.6±2.9 (3.1, 4.1)
SG >180 mg/dL (%)	29.0±7.4 (27.9, 30.2)	32.3±7.6 (31.1, 33.5)	3.3±1.7 (3.0, 3.6)	24.7±8.2 (23.3, 26.1)	27.5±8.4 (26.1, 29.0)	2.8±1.7 (2.5, 3.1)
SG >250 mg/dL (%)	6.8±3.7 (6.2, 7.3)	8.0±4.2 (7.3, 8.6)	1.2±1.1 (1.1, 1.4)	4.1±2.9 (3.6, 4.6)	4.9±3.4 (4.4, 5.5)	0.8±0.8 (0.7, 0.9)
SG >350 mg/dL (%)	0.6±0.7 (0.5, 0.7)	0.7±0.8 (0.5, 0.8)	0.0±0.3 (-0.0, 0.1)	0.2±0.3 (0.2, 0.3)	0.3±0.4 (0.2, 0.3)	0.0±0.1 (0.0, 0.1)
*Values are presented by Mean ± SD (95% CI) except for number of bolus events						

3. Pediatric Extrapolation

As described above in section A. Study Design, the clinical data include pediatrics down to 7 years of age. Therefore, other existing pediatric data was not leveraged.

Pivotal Study: Performance Evaluation of an Advanced Algorithm with CGM in Adults, Adolescents, and Pediatrics

Medtronic performed a clinical study to establish a reasonable assurance of safety and effectiveness of the Guardian Sensor (3) with the 'G' algorithm (also known as the Zeus algorithm), included in the Guardian 4 transmitter.

The clinical study included subjects 7–80 years of age and data was collected using the Guardian Sensor (3). During this pivotal study, sensor data were collected using a blinded approach, where the current commercial Guardian Connect Transmitter was used as a recorder for data collection purposes. No real-time data communication occurred during the study as no display device was used. Sensor data was processed using the "G" algorithm (the algorithm in the Guardian 4 transmitter) and then analyzed.

A. Study Design

The study was a multi-center, randomly assigned, prospective single-sample correlational design without controls where subjects were randomly assigned to

sensor location and frequent sample testing (FST) day and frequent sample testing (FST) time.
During this pivotal study sensor data were collected in a blinded approach, where current commercial Guardian Connect Transmitter was used as a recorder for the purpose of data collection. There was no real time data communication during the study as no mobile application was used.

In this study, the current commercial Guardian Sensor (3) was used and was connected to a Guardian Connect Transmitter, which measured the raw sensor signals for processing through the "G" algorithm with various calibration schemes. Testing on human subjects was necessary to characterize the accuracy of Guardian Sensor (3) with the "G" algorithm. Sensor glucose values were not presented to the subjects and were not used to make any therapy decisions. During the study, venous blood glucose concentrations were measured periodically by a reference method (Yellow Springs Instrument, YSI™ 2300 STAT glucose analyzer). Prior to initiating the study, several calibration schemes were prespecified in the protocol and were independently assessed. At the end of the study, the applicant chose to process raw sensor data collected by the Guardian Connect Transmitters (MMT-7821) through the final "G" algorithm, using a zero-calibration scheme, for analysis against the study endpoints. These values were then compared to the reference method values in order to determine sensor accuracy.

The Guardian Sensor (3) hardware design is identical to the Guardian 4 sensor which is part of the Guardian 4 system. The Guardian Connect Transmitter used to collect the study data shares the same hardware design with the new Guardian 4 transmitter which is part of the Guardian 4 system, and the final "G" algorithm is embedded in the Guardian 4 transmitter. The retrospective alert rates calculated using the "G" algorithm are applicable to the MiniMed 780G system. Based on the devices used and the analyses conducted, it was determined that the device system used in this accuracy study is equivalent to the Guardian 4 system.
A total of 308 previously diagnosed type 1 or 2 diabetes subjects were enrolled in order to have 229 subjects including 122 subjects (18-80 years old), and 107 subjects (7-17 years old) complete the study. Accuracy data were calculated by comparing calibrated sensor glucose values to a "gold standard" plasma glucose reference method (YSI™) for subjects 7-80 years old only), during frequent sample testing (FST).

The study conclusions support the accuracy of the Guardian Sensor (3) utilizing the "G" algorithm (identical to the Guardian 4 sensor) in a 7-80-year-old population.

1. Clinical Inclusion and Exclusion Criteria

   Subjects were considered for enrollment in the study if they met all of the following criteria:

   General Inclusion Criteria

1. Individual is 7-80 years of age at time of enrollment
2. A clinical diagnosis of type 1 or 2 diabetes for a minimum of 6 months duration as determined via medical record or source documentation by an individual qualified to make a medical diagnosis
3. Adequate venous access as assessed by investigator or appropriate staff
4. Subjects participating in the high and low glucose challenges must have an insulin carbohydrate ratio(s) and insulin sensitivity ratio. Subjects without ratios may participate under observation only

Subjects were not permitted to enroll in the pivotal study if they met any of the exclusion criteria

Exclusion Criteria

1. Subject will not tolerate tape adhesive in the area of Guardian™ Sensor (3) placement as assessed by a qualified individual
2. Subject has any unresolved adverse skin condition in the area of sensor or device placement (e.g., psoriasis, rash, Staphylococcus infection)
3. Subject is actively participating in an investigational study (drug or device) wherein they have received treatment from an investigational study (drug or device) in the last 2 weeks
4. Subject is female and has a positive pregnancy screening test
5. Female of child-bearing age and who is sexually active should be excluded if she is not using a form of contraception deemed reliable by investigator
6. Subject is female and plans to become pregnant during the course of the study
7. Subject has had a hypoglycemic seizure within the past 6 months prior to enrollment
8. Subject has had hypoglycemia resulting in loss of consciousness within the past 6 months prior to enrollment
9. Subject has had an episode of diabetic ketoacidosis (DKA) within the past 6 months prior to enrollment
10. Subject has a history of a seizure disorder
11. Subject has central nervous system or cardiac disorder resulting in syncope
12. Subject has a history of myocardial infarction, unstable angina, coronary artery bypass surgery, coronary artery stenting, transient ischemic attack (TIA), cerebrovascular accident (CVA), angina, congestive heart failure, ventricular rhythm disturbances or thromboembolic disease
13. Subject has a hematocrit (Hct) lower than the normal reference range (please note that patients may use prior blood draw from routine care as long as done within 6 months of screening and report of lab placed with subject source documents)
14. Subject has a history of adrenal insufficiency
15. Subject is a member of the research staff involved with the study

2. Follow-up Schedule

Subjects ages 14–80 years were scheduled to make 12 visits to the clinical study site, including the Enrollment/Screening visit (visit 1) and Study and device training (visit 2). Whereas, subjects ages 7-13 years were scheduled to make 8 visits to the clinical study site, including the Enrollment/Screening visit (visit 1) and Study and device training (visit 2). Subjects wore the devices for up to a 7-day Training Period, followed by a 7-day Study Period. In the event that early sensor removal occurred during the Training Period, the subject could continue to the Study Period based on investigator discretion.

During the study period, subjects ages 14–80 years underwent 4 days of YSI FSTs, each FST was approximately 8 hours during the in-clinic visit, whereas, subjects ages 7-13 years underwent 2 days of YSI FST, each approximately 6 hours during the in-clinic visit. During the YSI FST, venous blood samples were drawn every 5-15 minutes and analyzed using the YSI.

3. Clinical Endpoints

The primary endpoint of the Accuracy Study was as follows:

- For accuracy with Zeus algorithm the Guardian™ Sensor (3) values were compared to YSI plasma glucose values during YSI FSTs. A within 20% mean agreement rate (±20 mg/dl when SG less than (<) 80 mg/dl), μ, between Guardian™ Sensor (3) values and YSI plasma glucose values during YSI FST days was evaluated against the null Hypothesis.

The secondary endpoints of the Accuracy Study included analyses against the iCGM Special Controls.

Other study endpoints included:

- Precision Analysis: Sensor precision analysis was performed for the two sensors worn by the same subject in the same location
- Device survival based on physical sensor wear (0 to 170 hours) and functional sensor life (0 hours to 168 hours)
- Retrospective alert analysis; and
- Safety, as determined by adverse events and skin/insertion site reactions.

B. Accountability of Study Cohort

A total of 308 subjects were enrolled in the study; a total of 17 subjects discontinued during the course of the study; 5 subjects could not complete the study since the in-clinic research visits were discontinued due to COVID-19. A total of 267 subjects completed the study.

C. Study Population Demographics and Baseline Parameters

The study enrolled 308 previously diagnosed type 1 and 2 diabetic subjects. Subjects were grouped by age, diabetes classification, body mass index

(BMI)/weight, CGM experience, glycosylated hemoglobin (HbA1c), exercise activity, and compression procedure. The final study population demographics for this study are provided in Table 16 below.

Table 16: Study Demographics

Characteristic	Subjects 7-17 years of age Number of Subjects =115	Subjects 18-80 years of age Number of Subjects =169
Age (Years)		
n	115	169
Mean (SD)	12.4 (2.9)	45.9 (17.8)
Gender, N (%)		
Female	52 (45.2%)	91 (53.8%)
Male	63 (54.8%)	78 (46.2%)
Race, N (%)		
Asian	None	8 (4.7%)
Black or African American	6 (5.2%)	7 (4.1%)
Native Hawaiian/ Other Pacific Islander	None	1 (0.6%)
White	105 (91.3%)	143 (84.6%)
Other race	1 (0.9%)	6 (3.6%)
American Indian or Alaska Native; Black or African American	None	1 (0.6%)
White; Other race	None	1 (0.6%)
Asian; Other race	None	1 (0.6%)
Asian; White	3 (2.6%)	None
Black or African American; White	None	1 (0.6%)
Ethnicity N (%)		
Hispanic Or Latino	13 (11.3%)	21 (12.4%)
Not Hispanic Or Latino	102 (88.7%)	148 (87.6%)
Diabetes Type (%)		
Type 1 insulin requiring	115 (100.0%)	109 (64.5%)
Type 2 insulin requiring	None	32 (18.9%)
Type 2 non-insulin requiring	None	28 (16.6%)
Diabetes History (Years)		
n	115	169
Mean (SD)	5.8 (3.5)	17.6 (11.6)
Height (cm)		
n	115	169
Mean (SD)	155.5 (15.9)	169.4 (11.1)
Weight (kg)		
n	115	169
Mean (SD)	52.2 (17.2)	85.9 (21.0)
Body Mass Index (kg/m^2)		
n	115	169

Characteristic	Subjects 7-17 years of age Number of Subjects =115	Subjects 18-80 years of age Number of Subjects =169
Mean (SD)	20.9 (4.1)	30.0 (7.0)
Baseline A1C (%)		
n	115	169
Mean (SD)	8.5 (1.4)	7.8 (1.4)

D. Safety and Effectiveness Results for Guardian 4 Sensor with Guardian 4 Transmitter

1. Safety Results

The safety of the Guardian 4 Sensor and Guardian 4 Transmitter were assessed by evaluation of the incidence of all adverse events, serious Adverse Events (AEs), Adverse Device Events (ADEs), Serious Adverse Device Events (SADEs), and Unanticipated Adverse Device Effects (UADEs) experienced by study subjects. Adverse events (AEs) were listed in terms of severity and relationship to the device. Sensor insertion site and adhesive area were examined for erythema, edema and infection. The local skin reactions from the insertion site or adhesive were also evaluated.

Adverse Events for Subjects Ages 7-17 years

A total of 33 adverse events (AEs) and one serious adverse event were reported from all investigational sites for 7–17-year-old study subjects enrolled in the study. There was one incidence of diabetic ketoacidosis, and four incidences of severe hyperglycemia reported by the investigators. There were no device-related or procedure-related serious adverse events, or unanticipated adverse device effects after seven days of use.

Adverse Events for Subjects Ages 18-80 Years of Age

A total of 45 adverse events (AEs) and two serious adverse events were reported from all investigational sites for 18–80-year-old study subjects enrolled in the study. Out of 45 events, nine events were device related, and one each hypoglycemia and hyperglycemia events were reported which were non-device related. There were no reports of diabetic ketoacidosis events. There were no device-related or procedure-related serious adverse events, or unanticipated adverse device effects after seven days of use.

Skin Assessment

There were a total of 1043 skin assessments conducted on 166 subjects. The majority of skin observations were related to observations at the insertion site, including red and pink dots, raised areas or bumps around the insertion site and a drop of blood at the insertion site. The severity of these observations was

predominantly mild. There were 2 incidents of moderate redness in the area of the adhesive.

2. Effectiveness Results

1. Guardian 4 Sensor Performance: Pivotal Study (G190047)

Data collected during the study was post-processed after the study using the zero-calibration algorithm to convert the raw sensor information to sensor glucose values every five minutes. For the accuracy information presented in the following Table 17, YSI® or fingerstick reference values (Comparator Method, or CM) were paired with the closest sensor glucose reading within five minutes of the time of the reference value measurement. Sensor accuracy was calculated for sensors a YSI® reference for subjects ages 7 years and older.

Table 17: Overall Accuracy Compared to CM

Patient Population	Insertion Site	Number of Subjects	Number of paired SG-CM	Percent of SG within 20/20% of CM	MARD (%)
Adults (18+)	Arm	153	20612	88.3 (88.0)	10.6
Pediatrics (7-17)	Arm	107	7702	85.6 (85.0)	11.6

Table 18 and Table 19 present the agreement of the SG values to paired CM values which was assessed by calculating the percentage of CM values that were within 15%, 20%, and 40% of the paired SG values for the pediatric and adult populations based on sensor insertions sites. For CM readings less than 70 mg/dL, the absolute difference in mg/dL between the SG and paired CM values was calculated.

Table 18: Overall accuracy of SG-CM paired points within SG ranges; Adults, Arm

CGM Glucose Range (mg/dL)	Number of Subjects	Number of paired CGM-CM	Percent within 15 mg/dL CM*	Percent within 20 mg/dL CM*	Percent within 40 mg/dL CM*	Percent within 15% CM	Percent within 20% CM	Percent within 40% CM	Bias (mg/dL)	MARD (%)
A) <54 mg/dL	46	252	77.4	87.7	98.0				-9.3	14.9
B) 54-69 mg/dL	99	2204	91.0	95.9	99.7				-2.3	10.2
C) 70-180 mg/dL	153	12893				72.7	84.1	98.6	-4.9	11.3
D) 181-250 mg/dL	146	3857				81.6	91.1	99.7	-11.4	9.3
E) >250 mg/dL	97	1406				86.5	94.5	99.9	-7.3	8.2

* For reference range < 70 mg/dL, agreement was based on 15/20/30/40 mg/dL. CGM readings are within 50-400 mg/dL, inclusive

*Table 19: Overall accuracy of SG-CM paired points within SG ranges; Pediatrics**, Arm*

CGM Glucose Range (mg/dL)	Number of Subjects	Number of paired CGM-CM	Percent within 15 mg/dL CM*	Percent within 20 mg/dL CM*	Percent within 40 mg/dL CM*	Percent within 15% CM	Percent within 20% CM	Percent within 40% CM	Bias (mg/dL)	MARD (%)
A) <54 mg/dL	28	103	62.1	78.6	98.1				-13.0	19.4
B) 54-69 mg/dL	53	562	79.2	89.1	98.9				-6.3	12.9
C) 70-180 mg/dL	106	3967				64.6	79.2	98.4	-9.6	13.1
D) 181-250 mg/dL	103	1992				78.6	90.2	99.9	-14.1	9.9

CGM Glucose Range (mg/dL)	Number of Subjects	Number of paired CGM-CM	Percent within 15 mg/dL CM*	Percent within 20 mg/dL CM*	Percent within 40 mg/dL CM*	Percent within 15% CM	Percent within 20% CM	Percent within 40% CM	Bias (mg/dL)	MARD (%)
E) >250 mg/dL	77	1078				86.9	94.4	100.0	-8.0	8.3

* For reference range <70 mg/dL, agreement was based on 15/20/30/40 mg/dL.

**Includes pediatric subjects 7–17 years of age. CGM readings are within 50–400 mg/dL, inclusive

2. ***Agreement when CGM reads "Below 50 mg/dL" or "Above 400 mg/dL"***

The real-time CGM systems display glucose values between 50 mg/dL and 400 mg/dL. It displays "Below 50 mg/dL" when the SG value detected is below 50 mg/dL. It displays "Above 400 mg/dL" when the SG value detected is above 400 mg/dL. Table 20 and Table 21 illustrate the number and percentage of the paired YSI® values in different blood glucose levels when the CGM system displays "Below 50 mg/dL" (LOW) or "Above 400 mg/dL" (HIGH).

Table 20: The number and percentage of CM values collected when CGM displays 'Below 50 mg/dL' (LOW)

CGM Display	Population	Insertion Site	CGM-CM Pairs	CM (mg/dL)					
				<50	<60	<70	<80	280	Total
LOW	Adult	Arm	Cumulative, n	128	263	445	481	9	490
			Cumulative %	26%	54%	91%	98%	2%	
	Pediatrics *	Arm	Cumulative, n	51	87	168	194	6	200
			Cumulative %	26%	44%	84%	97%	3%	

*Includes pediatric subjects 7–17 years of age.

Table 21: The number and percentage of CM values collected when CGM displays 'Above 400 mg/dL' (HIGH)

CGM Display	Population	Insertion Site	CGM-CM Pairs	CM (mg/dL)					
				>400	>320	>280	>240	:'.240	Total
HIGH	Adult	Arm	Cumulative,	20	21	21	21	0	21
			Cumulative	95%	100%	100%	100%	0%	
	Pediatrics*	Arm	Cumulative,	32	32	32	32	0	32
			Cumulative	100%	100%	100%	100%	0%	

*Includes pediatric subjects 7–17 years of age.

3. ***Concurrence of SG and CM values***

Table 22 and Table 23 show, for each SG range, the percentage of concurring data points where the paired CM values were in different blood glucose ranges.

Table 22: Overall Concurrence of CM values and SG readings using SG Ranges; Adults, Arm

Percent of Matched Pairs in Each SMBG Glucose Range for Each SG Range (mg/dL)												
SG Ranges (mg/dL)	**Number of paired SG-CM**	**CM Glucose Range (mg/dL)**										
		<50	≥50– 60	>60– 80	>80–120	>120–160	>160–200	>200–250	>250–300	>300–350	>350–400	>400
A) <50	490	6.7% (33/490)	47.6% (233/490)	43.9% (215/490)	1.8% (9/490)	0.0% (0/490)	0.0% (0/490)	0.0% (0/490)	0.0% (0/490)	0.0% (0/490)	0.0% (0/490)	0.0% (0/490)
B) ≥50–60	1036	7.0% (73/1036)	38.4% (398/1036)	50.8% (526/1036)	3.5% (36/1036)	0.1% (1/1036)	0.2% (2/1036)	0.0% (0/1036)	0.0% (0/1036)	0.0% (0/1036)	0.0% (0/1036)	0.0% (0/1036)
C) >60–80	2899	0.5% (15/2899)	17.8% (517/2899)	69.7% (2022/2899)	11.6% (335/2899)	0.2% (6/2899)	0.1% (4/2899)	0.0% (0/2899)	0.0% (0/2899)	0.0% (0/2899)	0.0% (0/2899)	0.0% (0/2899)
D) >80–120	4334	0.0% (2/4334)	0.7% (31/4334)	12.7% (552/4334)	63.0% (2730/4334)	22.5% (973/4334)	1.0% (43/4334)	0.1% (3/4334)	0.0% (0/4334)	0.0% (0/4334)	0.0% (0/4334)	0.0% (0/4334)
E) >120–160	5123	0.0% (0/5123)	0.0% (0/5123)	0.1% (6/5123)	11.8% (604/5123)	63.8% (3271/5123)	22.0% (1129/5123)	2.0% (105/5123)	0.2% (8/5123)	0.0% (0/5123)	0.0% (0/5123)	0.0% (0/5123)
F) >160–200	3337	0.0% (0/3337)	0.0% (0/3337)	0.0% (0/3337)	0.3% (10/3337)	13.4% (447/3337)	57.5% (1920/3337)	25.7% (856/3337)	2.8% (95/3337)	0.3% (9/3337)	0.0% (0/3337)	0.0% (0/3337)
G) >200–250	2477	0.0% (0/2477)	0.0% (0/2477)	0.0% (0/2477)	0.0% (0/2477)	0.3% (7/2477)	11.7% (291/2477)	61.1% (1514/2477)	23.8% (589/2477)	3.0% (74/2477)	0.1% (2/2477)	0.0% (0/2477)
H) >250–300	895	0.0% (0/895)	0.0% (0/895)	0.0% (0/895)	0.0% (0/895)	0.0% (0/895)	0.0% (0/895)	13.7% (123/895)	56.3% (504/895)	27.7% (248/895)	2.2% (20/895)	0.0% (0/895)

Percent of Matched Pairs in Each SMBG Glucose Range for Each SG Range (mg/dL)												
I) >300–350	390	0.0% (0/390)	0.0% (0/390)	0.0% (0/390)	0.0% (0/390)	0.0% (0/390)	0.0% (0/390)	1.0% (4/390)	25.4% (99/390)	55.4% (216/390)	16.7% (65/390)	1.5% (6/390)
J) >350–400	121	0.0% (0/121)	0.0% (0/121)	0.0% (0/121)	0.0% (0/121)	0.0% (0/121)	0.0% (0/121)	0.0% (0/121)	1.7% (2/121)	36.4% (44/121)	51.2% (62/121)	10.7% (13/121)
K) >400	21	0.0% (0/21)	0.0% (0/21)	0.0% (0/21)	0.0% (0/21)	0.0% (0/21)	0.0% (0/21)	0.0% (0/21)	0.0% (0/21)	4.8% (1/21)	52.4% (11/21)	42.9% (9/21)

Table 23: Overall Concurrence of CM Values and SG Readings Using SG Ranges; Pediatrics, Arm*

Percent of Matched Pairs in Each CM Glucose Range for Each SG Range (mg/dL)												
SG Ranges (mg/dL)	**Number of Paired SG-CM**	**CM Glucose Ranges (mg/dL)**										
		<50	≥50– 60	>60– 80	>80–120	>120–160	>160–200	>200–250	>250–300	>300–350	>350–400	>400
A) <50	200	11.5% (23/200)	32.5% (65/200)	53.0% (106/200)	2.5% (5/200)	0.5% (1/200)	0.0% (0/200)	0.0% (0/200)	0.0% (0/200)	0.0% (0/200)	0.0% (0/200)	0.0% (0/200)
B) ≥50–60	346	4.0% (14/346)	26.0% (90/346)	64.2% (222/346)	5.2% (18/346)	0.6% (2/346)	0.0% (0/346)	0.0% (0/346)	0.0% (0/346)	0.0% (0/346)	0.0% (0/346)	0.0% (0/346)
C) >60–80	692	0.7% (5/692)	13.4% (93/692)	61.6% (426/692)	23.6% (163/692)	0.7% (5/692)	0.0% (0/692)	0.0% (0/692)	0.0% (0/692)	0.0% (0/692)	0.0% (0/692)	0.0% (0/692)
D) >80–120	1348	0.1% (1/1348)	1.2% (16/1348)	12.5% (168/1348)	57.0% (768/1348)	27.8% (375/1348)	1.4% (19/1348)	0.1% (1/1348)	0.0% (0/1348)	0.0% (0/1348)	0.0% (0/1348)	0.0% (0/1348)
E) >120–160	1529	0.0% (0/1529)	0.0% (0/1529)	0.1% (1/1529)	7.5% (114/1529)	58.3% (891/1529)	30.0% (458/1529)	3.4% (52/1529)	0.8% (12/1529)	0.1% (1/1529)	0.0% (0/1529)	0.0% (0/1529)

Percent of Matched Pairs in Each CM Glucose Range for Each SG Range (mg/dL)												
F) >160–200	1439	0.0% (0/1439)	0.0% (0/1439)	0.0% (0/1439)	0.1% (1/1439)	9.0% (129/1439)	51.4% (739/1439)	35.9% (516/1439)	3.3% (48/1439)	0.3% (5/1439)	0.0% (0/1439)	0.0% (0/1439)
G) >200–250	1270	0.0% (0/1270)	0.0% (0/1270)	0.0% (0/1270)	0.0% (0/1270)	0.2% (3/1270)	9.9% (126/1270)	59.4% (754/1270)	28.7% (364/1270)	1.8% (23/1270)	0.0% (0/1270)	0.0% (0/1270)
H) >250–300	695	0.0% (0/695)	0.0% (0/695)	0.0% (0/695)	0.0% (0/695)	0.0% (0/695)	0.1% (1/695)	13.1% (91/695)	58.6% (407/695)	25.8% (179/695)	2.4% (17/695)	0.0% (0/695)
I) >300–350	296	0.0% (0/296)	0.0% (0/296)	0.0% (0/296)	0.0% (0/296)	0.0% (0/296)	0.0% (0/296)	1.0% (3/296)	18.9% (56/296)	61.1% (181/296)	18.9% (56/296)	0.0% (0/296)
J) >350–400	87	0.0% (0/87)	0.0% (0/87)	0.0% (0/87)	0.0% (0/87)	0.0% (0/87)	0.0% (0/87)	0.0% (0/87)	5.7% (5/87)	24.1% (21/87)	60.9% (53/57)	9.2% (8/87)
K) >400	32	0.0% (0/32)	0.0% (0/32)	0.0% (0/32)	0.0% (0/32)	0.0% (0/32)	0.0% (0/32)	0.0% (0/32)	0.0% (0/32)	0.0% (0/32)	31.3% (10/32)	68.8% (22/32)

*Includes pediatric subjects 7–17 years of age.

4. ***Trend Accuracy***

A summary of the Guardian 4 CGM trend accuracy in the adult population with the arm insertion location is shown in Table 24 below. The top right and bottom left corners of the table represent the areas where there is the most incongruence between the SG rate of change and the CM rate of change. There was only one point where the SG rate of change was less than -1 mg/dL/min and the CM rate of change was greater than 1 mg/dL/min. Similarly, there were only five points where the SG rate of change was greater than 1 mg/dL/min and the CM rate of change was less than -1 mg/dL/min.

Table 24: Trend Accuracy Compared to CM Over Time; Adults; Arm

CGM Rate Ranges (mg/dL/min)	**Percent of Matched Pairs-in Each CM Rate Range for Each CGM Rate Range CM (mg/dL/min)**						
	Number of Paired CGM-CM	**<-2**	**[-2, -1)**	**[-1, 0)**	**[0, 1]**	**(1, 2]**	**>2**
<-2	179	53.6% (96/179)	38.0% (68/179)	7.3% (13/179)	1.1% (2/179)	0.0% (0/179)	0.0% (0/179)
[-2, -1)	1036	5.2% (54/1036)	49.9% (517/1036)	42.3% (438/1036)	2.5% (26/1036)	0.1% (1/1036)	0.0% (0/1036)
[-1, 0)	10059	0.2% (17/10059)	4.0% (401/10059)	79.1% (7958/10059)	16.3% (1640/10059)	0.4% (37/10059)	0.1% (6/10059)
[0, 1]	7342	0.0% (3/7342)	0.5% (38/7342)	22.6% (1656/7342)	69.9% (5129/7342)	6.6% (487/7342)	0.4% (29/7342)
(1, 2]	1513	0.0% (0/1513)	0.3% (5/1513)	2.0% (31/1513)	29.5% (446/1513)	58.6% (886/1513)	9.6% (145/1513)
>2	461	0.0% (0/461)	0.0% (0/461)	0.4% (2/461)	4.3% (20/461)	37.5% (173/461)	57.7% (266/461)

CGM readings are within 50–400 mg/dL, inclusive.

A summary of the Guardian 4 sensor trend accuracy in the pediatric population (7-17 years) with the arm insertion location is shown in Table 25 below. The top right and bottom left corners of the table represent the areas where there is the most incongruence between the SG rate of change and the CM rate of change. There were only six points where the SG rate of change was less than -1 mg/dL/min and the CM rate of change was greater than 1 mg/dL/min.

Table 25: Trend Accuracy Compared to CM over time; Pediatrics, Arm*

CGM Rate Ranges (mg/dL/min)	Percent of Matched Pairs-in Each CM Rate Range for Each CGM Rate Range						
	CM (mg/dL/min)						
	Number of Paired CGM-CM	<-2	[-2, -1)	[-1, 0)	[0, 1]	(1, 2]	>2
<-2	196	50.5% (99/196)	41.3% (81/196)	7.1% (14/196)	1.0% (2/196)	0.0% (0/196)	0.0% (0/196)
[-2, -1)	742	6.2% (46/742)	53.6% (398/742)	36.7% (272/742)	2.7% (20/742)	0.7% (5/742)	0.1% (1/742)
[-1, 0)	3103	0.3% (9/3103)	6.5% (201/3103)	76.2% (2363/3103)	15.8% (490/3103)	1.0% (31/3103)	0.3% (9/3103)
[0, 1]	2450	0.0% (1/2450)	0.9% (23/2450)	21.1% (517/2450)	68.6% (1680/2450)	8.9% (218/2450)	0.4% (11/2450)
(1, 2]	851	0.0% (0/851)	0.1% (1/851)	3.1% (26/851)	32.2% (274/851)	55.9% (476/851)	8.7% (74/851)
>2	354	0.0% (0/354)	0.0% (0/354)	0.3% (1/354)	4.2% (15/354)	28.0% (99/354)	67.5% (239/354)

CGM readings are within 50–400 mg/dL, inclusive.
*Includes pediatric subjects 7–17 years of age.

5. ***Sensor Accuracy Over Time***

A summary of the Guardian 4 sensor stability and accuracy over time throughout early-wear, mid-wear, and late wear in the adult population with the arm insertion site is shown in Table 26 below. All 40/40 agreement rates were above 98% with most above 99%.

Table 26: Sensor Accuracy Compared to CM Over Time; Adults, Arm

Wear Period	Number of paired SG-CM	Percent of CM within 15/15% of CM (%)*	Percent of CM within 20/20% of CM (%)*	Percent of CM within 40/40% of CM (%)*	Mean Absolute Relative Difference (%)
Beginning	5678	65.8	78.3	98.3	13.9
Early	5504	80.9	91	99.7	10.0
Late Middle	5142	81.0	91.5	99.7	9.7
End	4288	87.5	94.4	99.7	8.3

CGM readings are within 50–400 mg/dL, inclusive.
*For reference range < 70 mg/dL, agreement was based on 15/20/40 mg/dL.

A summary of the Guardian 4 sensor stability and accuracy over time throughout early-wear, mid-wear, and late wear in the pediatric population (7-17 years) with the arm insertion site is shown in Table 27 below. All 40/40 agreement rates were above 98% with most above 99%.

*Table 27: Sensor Accuracy Compared to CM Over Time; Pediatrics**, Arm*

Wear Period	Number of paired SG-CM	Percent of CM within 15/15% of CM (%)*	Percent of CM within 20/20% of CM (%)*	Percent of CM within 40/40% of CM (%)*	Mean Absolute Relative Difference (%)
Beginning	3127	68.5	84.7	99.5	12.8
Early	2546	74.4	85.5	98.9	11.5
Late Middle	1145	74.8	84.3	99.8	10.9
End	884	81.7	91.0	99.8	9.1

**Includes pediatric subjects 7–17 years of age.
CGM readings are within 50–400 mg/dL, inclusive.
*For reference range < 70 mg/dL, agreement was based on 15/20/40 mg/dL.

6. ***Pump Alert Performance with 780G System with Guardian 4 CGM- Arm Insertion***

Alert performance was evaluated to obtain 'true alert' and 'false alert' rates, and 'correctly detected' and 'missed detection' rates. The descriptions and Table 28 – Table 35 below describe the alert rate performance of the device within this clinical study:

Glucose True alert rates

The true alert rate is the rate at which the blood glucose value confirmed that the continuous glucose monitor alert was triggered correctly. The default threshold alerts are highlighted in gray in the tables below. For example:

- True Threshold Hypoglycemic alert rate alerted when the continuous glucose monitor read that the user was below the low threshold and the user's blood glucose was actually below that low threshold (within +/- 15 or 30 minutes of the alert)
- True Threshold Hyperglycemic alert rate alerted when the continuous glucose monitor read that the user was above the high threshold and the user's blood glucose was actually above that high threshold (within +/- 15 or 30 minutes of the alert)
- True Predictive Hypoglycemic alert rate alerted when the continuous glucose monitor predicted that the user would reach below the low threshold and the user's blood glucose was actually below that low threshold within 15 or 30 minutes following the alert
- True Predictive Hyperglycemic alert rate alerted when the continuous

glucose monitor predicted that the user would reach above the high threshold and the user's blood glucose was actually above that high threshold within 15 or 30 minutes following the alert.

Table 28: Glucose TRUE Alert Performance, Adults

Glucose TRUE Alert Rate							
mg/dL	**Insertion Site**	**Threshold Only**		**Predictive Only**		**Threshold and Predictive**	
		30 min	**15 min**	**30 min**	**15 min**	**30 min**	**15 min**
50	Arm	27.3%	25.8%	28.3%	19.9%	28.0%	21.6%
60	Arm	73.3%	71.9%	57.4%	53.0%	63.2%	59.9%
64	Arm	83.0%	82.4%	-	-	-	-
70	Arm	85.9%	85.9%	64.1%	60.3%	72.4%	70.1%
80	Arm	81.9%	80.8%	62.2%	58.9%	70.0%	67.6%
90	Arm	77.7%	77.4%	59.8%	57.0%	66.9%	65.1%
180	Arm	87.6%	87.2%	66.4%	64.0%	74.3%	72.7%
220	Arm	86.8%	86.8%	64.2%	62.1%	72.2%	70.9%
250	Arm	87.9%	87.0%	67.3%	62.0%	74.5%	70.8%
300	Arm	88.9%	88.9%	69.5%	65.5%	76.1%	73.5%

The default alert threshold is highlighted in grey.

*Table 29: Glucose TRUE Alert Performance, Pediatrics**

Glucose TRUE Alert Rate							
mg/dL	**Insertion Site**	**Threshold Only**		**Predictive Only**		**Threshold and Predictive**	
		30 min	**15 min**	**30 min**	**15 min**	**30 min**	**15 min**
50	Arm	23.8%	23.8%	13.3%	9.2%	16.4%	13.6%
60	Arm	52.8%	52.8%	34.3%	32.9%	40.6%	39.6%
64	Arm	59.2%	59.2%	-	-	-	-
70	Arm	63.0%	63.0%	44.6%	40.8%	51.1%	48.6%
80	Arm	69.1%	69.1%	50.0%	44.5%	57.1%	53.6%
90	Arm	74.4%	72.2%	56.3%	51.7%	63.6%	60.0%
180	Arm	92.2%	92.2%	82.7%	78.3%	86.8%	84.3%
220	Arm	91.3%	90.2%	77.3%	74.0%	83.0%	80.5%
250	Arm	88.4%	88.4%	70.7%	68.4%	77.4%	75.9%
300	Arm	85.2%	85.2%	60.5%	59.9%	68.9%	68.5%

* Includes pediatric subjects 7–17 years of age.
The default alert threshold is highlighted in grey.

Glucose False Alert Rates

The glucose false alert rate is the rate at which the blood glucose value did not confirm that the continuous glucose monitor alert was triggered correctly. For example:

- False Threshold Hypoglycemic alert rate the alarm alerted when the continuous glucose monitor read that the user was below the low threshold but the users blood glucose was actually above that low threshold (within +/- 15 or 30 minutes of the alert).
- False Threshold Hyperglycemic alert rate the alarm alerted when the continuous glucose monitor read that the user was above the high threshold but the user's blood glucose was actually below that high threshold (within +/- 15 or 30 minutes of the alert).
- False Predictive Hypoglycemic alert rate the alarm alerted when the continuous glucose monitor predicted that the user would be below the low threshold but the user's blood glucose was actually above that low threshold within 15 or 30 minutes following the alert.
- False Predictive Hyperglycemic alert rate the alarm alerted when the continuous glucose monitor predicted that the user would be above the high threshold but the user's blood glucose was actually below the high threshold within 15 or 30 minutes following the alert.

Table 30: Glucose FALSE Alert Performance, Adults

Glucose FALSE Alert Rate							
mg/dL	**Insertion Site**	**Threshold Only**		**Predictive Only**		**Threshold and Predictive**	
		30 min	**15 min**	**30 min**	**15 min**	**30 min**	**15 min**
50	Arm	72.7%	74.2%	71.7%	80.1%	72.0%	78.4%
60	Arm	26.7%	28.1%	42.6%	47.0%	36.8%	40.1%
64	Arm	17.0%	17.6%	-	-	-	-
70	Arm	14.1%	14.1%	35.9%	39.7%	27.6%	29.9%
80	Arm	18.1%	19.2%	37.8%	41.1%	30.0%	32.4%
90	Arm	22.3%	22.6%	40.2%	43.0%	33.1%	34.9%
180	Arm	12.4%	12.8%	33.6%	36.0%	25.7%	27.3%
220	Arm	13.2%	13.2%	35.8%	37.9%	27.8%	29.1%
250	Arm	12.1%	13.0%	32.7%	38.0%	25.5%	29.2%
300	Arm	11.1%	11.1%	30.5%	34.5%	23.9%	26.5%

The default alert threshold is highlighted in grey.

*Table 31: Glucose FALSE Alert Performance, Pediatrics**

Glucose FALSE Alert Rate							
mg/dL	**Insertion Site**	**Threshold Only**		**Predictive Only**		**Threshold and Predictive**	
		30 min	**15 min**	**30 min**	**15 min**	**30 min**	**15 min**
50	Arm	76.2%	76.2%	86.7%	90.8%	83.6%	86.4%
60	Arm	47.2%	47.2%	65.7%	67.1%	59.4%	60.4%
64	Arm	40.8%	40.8%	-	-	-	-
70	Arm	37.0%	37.0%	55.4%	59.2%	48.9%	51.4%
80	Arm	30.9%	30.9%	50.0%	55.5%	42.9%	46.4%
90	Arm	25.6%	27.8%	43.7%	48.3%	36.4%	40.0%
180	Arm	7.8%	7.8%	17.3%	21.7%	13.2%	15.7%
220	Arm	8.7%	9.8%	22.7%	26.0%	17.0%	19.5%
250	Arm	11.6%	11.6%	29.3%	31.6%	22.6%	24.1%
300	Arm	14.8%	14.8%	39.5%	40.1%	31.1%	31.5%

*Includes pediatric subjects 7–17 years of age.
The default alert threshold is highlighted in grey.

Glucose Correct Detection Rates

Glucose Correct Detection Rate is the rate that the device alerted when it should have alerted. For example, the blood glucose was below the hypoglycemic threshold, or above the hyperglycemic threshold, and the device sounded an alert (within +/- 15 or 30 minutes for the threshold alerts, and within 15 or 30 minutes following predictive alerts).

Table 32: Glucose CORRECT DETECTION Performance, Adults

Glucose CORRECT DETECTION Rate							
mg/dL	**Insertion Site**	**Threshold Only**		**Predictive Only**		**Threshold and Predictive**	
		30 min	**15 min**	**30 min**	**15 min**	**30 min**	**15 min**
50	Arm	37.5%	35.4%	89.6%	72.9%	89.6%	79.2%
60	Arm	65.1%	64.0%	86.0%	83.7%	86.6%	84.3%
64	Arm	75.5%	75.0%	-	-	-	-
70	Arm	87.3%	86.8%	94.8%	93.4%	95.3%	94.3%
80	Arm	84.2%	83.1%	91.4%	86.8%	91.4%	88.7%
90	Arm	87.3%	86.3%	93.3%	90.2%	93.7%	91.7%
180	Arm	83.0%	81.8%	94.2%	90.4%	94.4%	91.3%
220	Arm	79.4%	78.3%	92.4%	90.6%	92.7%	90.9%
250	Arm	72.5%	71.1%	88.3%	85.3%	88.3%	86.1%

Glucose CORRECT DETECTION Rate							
300	Arm	62.3%	60.1%	83.3%	80.4%	83.3%	80.4%

The default alert threshold is highlighted in grey.

*Table 33: Glucose CORRECT DETECTION Performance, Pediatrics**

Glucose CORRECTION DETECTION Rate							
mg/dL	**Insertion Site**	**Threshold Only**		**Predictive Only**		**Threshold and Predictive**	
		30 min	**15 min**	**30 min**	**15 min**	**30 min**	**15 min**
50	Arm	66.7%	66.7%	86.7%	60.0%	86.7%	73.3%
60	Arm	64.6%	64.6%	80.0%	75.4%	80.0%	76.9%
64	Arm	74.6%	74.6%	-	-	-	-
70	Arm	83.3%	81.0%	92.9%	86.9%	92.9%	91.7%
80	Arm	86.6%	85.7%	97.3%	89.3%	97.3%	92.9%
90	Arm	89.9%	87.9%	97.3%	89.9%	98.0%	93.3%
180	Arm	90.3%	89.0%	96.2%	91.3%	96.9%	94.1%
220	Arm	88.0%	84.9%	95.9%	92.1%	96.2%	94.5%
250	Arm	77.1%	74.8%	91.6%	85.0%	91.6%	87.4%
300	Arm	72.2%	72.2%	93.8%	88.7%	93.8%	89.7%

* Includes pediatric subjects 7–17 years of age.

The default alert threshold is highlighted in grey.

Glucose Missed Detection Rates

The Missed Detection Rate is the rate that the device did not alert when it should have (within +/- 15 or 30 minutes for the threshold alerts, and within 15 or 30 minutes following predictive alerts). For example, the blood glucose was below the hypoglycemic threshold, or above the hyperglycemic threshold, and the device did not sound a threshold or predictive alert.

Table 34: Glucose MISSED DETECTION Performance, Adults

Glucose MISSED DETECTION Rate							
mg/dL	**Insertion Site**	**Threshold Only**		**Predictive Only**		**Threshold and Predictive**	
		30 min	**15 min**	**30 min**	**15 min**	**30 min**	**15 min**
50	Arm	62.5%	64.6%	10.4%	27.1%	10.4%	20.8%
60	Arm	34.9%	36.0%	14.0%	16.3%	13.4%	15.7%
64	Arm	24.5%	25.0%	-	-	-	-
70	Arm	12.7%	13.2%	5.2%	6.6%	4.7%	5.7%

Glucose MISSED DETECTION Rate							
80	Arm	15.8%	16.9%	8.6%	13.2%	8.6%	11.3%
90	Arm	12.7%	13.7%	6.7%	9.8%	6.3%	8.3%
180	Arm	17.0%	18.2%	5.8%	9.6%	5.6%	8.7%
220	Arm	20.6%	21.7%	7.6%	9.4%	7.3%	9.1%
250	Arm	27.5%	28.9%	11.7%	14.7%	11.7%	13.9%
300	Arm	37.7%	39.9%	16.7%	19.6%	16.7%	19.6%

The default alert threshold is highlighted in grey.

*Table 35: Glucose MISSED DETECTION Performance, Pediatrics**

Glucose MISSED DETECTION Rate							
mg/dL	**Insertion Site**	**Threshold Only**		**Predictive Only**		**Threshold and Predictive**	
		30 min	**15 min**	**30 min**	**15 min**	**30 min**	**15 min**
50	Arm	33.3%	33.3%	13.3%	40.0%	13.3%	26.7%
60	Arm	35.4%	35.4%	20.0%	24.6%	20.0%	23.1%
64	Arm	25.4%	25.4%	-	-	-	-
70	Arm	16.7%	19.0%	7.1%	13.1%	7.1%	8.3%
80	Arm	13.4%	14.3%	2.7%	10.7%	2.7%	7.1%
90	Arm	10.1%	12.1%	2.7%	10.1%	2.0%	6.7%
180	Arm	9.7%	11.0%	3.8%	8.7%	3.1%	5.9%
220	Arm	12.0%	15.1%	4.1%	7.9%	3.8%	5.5%
250	Arm	22.9%	25.2%	8.4%	15.0%	8.4%	12.6%
300	Arm	27.8%	27.8%	6.2%	11.3%	6.2%	10.3%

*Includes pediatric subjects 7–17 years of age.
The default alert threshold is highlighted in grey.

7. ***Sensor Life***

Adults (18-75 years of age)

77.8% of sensors worn in the arm functioned more than six days and up to the full seven days of wear (144 to 168 hours). The median functional sensor life for sensors worn in the arm insertion site over the course of the study was 167.9 hours, with a mean functional life of 147.9 hours.

Pediatrics (7-17 years of age)

61.7% of sensors worn in the arm functioned more than six days and up to the full seven days of wear (144 to 168 hours). The median functional sensor life for sensors worn in the arm insertion site over the course of the study was 163.7 hours, with a mean functional life of 138.9 hours.

*8. **Precision Analysis***

Precision of the system was evaluated by comparing the results from two separate sensors worn in the location on the same subject at the same time. Table 36 provides the summary of a precision analysis.

Table 36: Precision Analysis

Age and Site of Insertion	Number of paired points	Percent Absolute Relative Difference (PARD)	Coefficient of variation (%CV)
7-17 YO Arm	10386	9.48	6.5
18+ YO Arm	23549	9.08	6.5

3. Pediatric Extrapolation

As described above in section A. Study Design, the clinical data include pediatrics down to 7 years of age. Therefore, other existing pediatric data was not leveraged.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation.

The AHCL pivotal study (G190075) included 19 principal investigators. The following clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f).

- Dr. Anders Carlson
- Dr. Kevin Kaiserman
- Dr. James Thrasher

The Guardian 4 sensor performance study (G190047) included 15 principal investigators. The following clinical investigator had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f).

- Dr. Kevin Kaiserman

The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Continued Access Study Period, CIP321 (G190075)

Subjects in the CIP321 pivotal study (G190075) were given the opportunity to continue using the investigational MiniMed 670G 4.0 system study devices for a period of up to 2 years after the end of the study period, or until the device became available commercially. During this continued access study (CAS) phase, subjects were scheduled for office visits at 90-day intervals beginning 90-days after the last study period visit and continuing until the end of the study. At each visit subjects were asked about adverse events and device complaints in addition to routine check-up questions.

During the CAS phase, subjects transitioned from the MiniMed 670G 4.0 system to the MiniMed 780G system with the Guardian 4 Transmitter and Guardian 4 Sensor intended for commercialization. The purpose of the CAS period was to provide long-term data on the system and to evaluate subject safety with use of the MiniMed 780G system.

Data from the CAS phase was collected from 176 subjects that transitioned from using the MiniMed 670G 4.0 system to the MiniMed 780G system with the Guardian 4 transmitter and Guardian 4 sensor in the CAS phase and completed their 90-day visit (+/- 14 days) or exited before their 90-day visit. The CAS phase of the study is still ongoing.

Study Population Demographics and Baseline Parameters

Demographics and additional baseline characteristics (at screening) for subjects who entered the continued access period and used the MiniMed 780G insulin pump with the Guardian 4 transmitter and Guardian 4 sensor were collected during the screening process of clinical study CIP321. The demographics of the study population are typical for studies performed in the Type 1 diabetes population performed in the US and are presented in Table 37.

Table 37: MiniMed 780G use Continued Access Study Demographics

Characteristic	Subjects 7-17 years old Number of Subjects = 109	Subjects 18-75 years old Number of Subjects = 67
Age (Years)		
n	109	67
Mean (SD)	11.2 (2.5)	45.4 (14.8)
Median	11.0	47.0
Min, Max	7.0, 17.0	18.0, 75.0
Gender N(%)		
Female	52 (47.7%)	36 (53.7%)
Male	57 (52.3%)	31 (46.3%)
Race N(%)		
White	97 (89.0%)	66 (98.5%)
Asian	2 (1.8%)	1 (1.5%)
Asian, White	3 (2.8%)	0 (0.0%)
Black/African	2 (1.8%)	0 (0.0%)

Characteristic	Subjects 7-17 years old Number of Subjects = 109	Subjects 18-75 years old Number of Subjects = 67
American		
Native Hawaiian or Other Pacific Islander	1 (0.9%)	0 (0.0%)
Other	4 (3.7%)	0 (0.0%)
Ethnicity N(%)		
Hispanic Or Latino	8 (7.3%)	3 (4.5%)
Not Hispanic Or Latino	101 (92.7%)	64 (95.5%)
Diabetes History (Years)		
n	109	67
Mean (SD)	6.6 (2.7)	27.1 (12.8)
Median	6.0	27.6
Min, Max	1.8, 15.0	6.1, 60.7
Height (cm)		
n	109	67
Mean (SD)	149.7 (15.2)	171.5 (9.7)
Median	151.0	170.2
Min, Max	116.2, 187.0	155.0, 191.7
Weight (kg)		
n	109	67
Mean (SD)	44.6 (13.4)	85.9 (20.2)
Median	42.0	84.8
Min, Max	21.4, 78.7	58.5, 165.9
BMI (Kg/m2)		
n	109	67
Mean (SD)	19.5 (3.3)	29.1 (5.8)
Median	18.7	27.8
Min, Max	14.7, 29.7	20.8, 51.2
Baseline (at screening) A1C (%)		
n	109	67
Mean (SD)	7.9 (0.9)	7.6 (0.8)
Median	7.9	7.5
Min, Max	6.1, 9.9	5.8, 9.8

Safety and Effectiveness Results

Safety Results

A total of 57 adverse events (AEs) were reported. Six were classified as device-related for all subjects who used the MiniMed 780G insulin pump with the Guardian 4 transmitter and Guardian 4 sensor during the CAS phase and either completed their 90--day visit (+/- 14 days) or exited before their 90-day visit. Table 38 below summarizes the number and type of AEs that were reported for the CAS phase with subject use of the MiniMed 780G insulin pump with the Guardian 4 transmitter and Guardian 4 sensor.

Of the five reported severe hyperglycemia events for subjects 7-17 years of age, one was thought to be device-related. One severe hyperglycemia event reported for subjects 18-75 years of age was thought to be device-related. Two device-related severe hyperglycemia events, one for 7-17-year-olds and one for 18-75-year-olds, reported were believed to be due to infusion set issues (i.e., occlusion, bent cannula or cannula pull out).

Table 38: Summary of Adverse Event Number and Type. MiniMed 780G System Continued Access Study

Adverse Event Type	Number of Adverse Events		
	7–17-year-old subjects (N=109)	18–75-year-old subjects (N=67)	Total
Number of adverse events	32	25	57
Death	0	0	0
Discontinuation due to adverse events	0	0	0
Study procedure-related adverse events	0	0	0
Study device-related adverse events	3	3	6
Serious adverse events	0	0	0
Severe hypoglycemia events*	0	0	0
Severe hyperglycemia events**	5	1	6
Diabetic ketoacidosis	0	0	0
Unanticipated adverse device effects	0	0	0
Unanticipated non-serious adverse device related evens	0	0	0

* Severe hypoglycemia was defined in the protocol as 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 they were unable to treat themself, were unable to verbalize their needs, and were incoherent, disoriented and/or combative.

** Severe hyperglycemia was defined in the protocol as hyperglycemia (blood glucose greater than (>) 300 mg/dL [16.7 mol/L]) with blood glucose ketones greater than (>) 1.5 mmol/L, urine ketones moderate or large, or accompanied by symptoms of nausea, vomiting or abdominal pain.

Effectiveness Results

The data below are from subjects that used the MiniMed 780G insulin pump with the Guardian 4 transmitter and Guardian 4 sensor during the CAS phase and either completed their 90-day visit (+/- 14 days) or exited before their 90-day visit.

Table 39 below provides an overall summary of the CAS phase for all subjects that

completed their 90-day visit (+/- 14 days) or exited before their 90-day visit of MiniMed 780G use with the Guardian 4 transmitter and Guardian 4 sensor. The data presented in this table includes information about subjects' glucose levels during the CAS phase. Both pediatric and adult subject groups spent greater than 70% percent of time in the target range (70-180 mg/dL), with a mean sensor glucose value of 153 mg/dL for subjects 7-17 years of age and 147.6 mg/dL for subjects 18-75 years of age.

Table 39: Sensor Glucose and Percent of Time within Glucose Ranges for 780G System use by Subjects during the Continued Access Study

Parameter	7–17-year-old subjects (N=109)	18–75-year-old subjects (N=67)
Sensor Glucose, (mg/dL) Mean (SD), (95% CI)	153.0 (13.0), (150.5, 155.5)	147.6 (13.6), (144.3, 150.9)
Sensor Glucose Range (mg/dL)	Percent of Time with Glucose Level in Range Mean ± SD (95% CI), %	
< 54 mg/dL	0.4 ± 0.4 (0.3, 0.5)	0.3 ± 0.3 (0.2, 0.3)
< 60 mg/dL	0.8 ± 0.7 (0.7, 1.0)	0.5 ± 0.5 (0.4, 0.7)
< 70 mg/dL	2.2 ± 1.4 (1.9, 2.4)	1.6 ± 1.1 (1.3, 1.8)
70–180 mg/dL	71.5 ± 7.8 (70.0, 73.0)	76.6 ± 9.0 (74.4, 78.8)
> 180 mg/dL	26.3 ± 8.1 (24.8, 27.9)	21.8 ± 9.3 (19.6, 24.1)
> 250 mg/dL	6.9 ± 4.5 (6.0, 7.7)	4.2 ± 3.8 (3.2, 5.1)
> 350 mg/dL	0.7 ± 1.1 (0.5, 0.9)	0.3 ± 0.5 (0.2, 0.4)

Subjects' HbA1c value was collected at the start of 780G use with the Guardian 4 transmitter and Guardian 4 sensor during the CAS phase and had another HbA1c value collected at the 90-day visit of the CAS phase. The mean change in HbA1c from the start of 780G use and the 90-day visit was analyzed and found to be -0.4% for subjects 7-17 years of age (with 95% confidence intervals of -0.6 to -0.3) and -0.3% for subjects 18-75 years of age (with 95% confidence intervals of -0.4 to -0.2). A summary of HbA1c data is provided in Table 40 below.

Table 40: Percent Change in HbA1c from Start of Continued Access Study with 780G System to 90-day visit of the CAS Phase

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	Start of CAS (SD)	90-day of CAS (SD)	Change from Baseline to 90-day of CAS (SD)	Start of CAS (SD)	90-day of CAS (SD)	Change from Baseline to 90-day of CAS (SD)
Number of Subjects	104	101	96	67	63	63
HbA1c, %, Mean (SD)	7.7 (0.9)	7.2 (0.7)	-0.4 (0.6)	7.1 (0.7)	6.8 (0.7)	-0.3 (0.4)
HbA1c, %,	7.6	7.1	-0.4	7.0	6.8	-0.2

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	Start of CAS (SD)	90-day of CAS (SD)	Change from Baseline to 90-day of CAS (SD)	Start of CAS (SD)	90-day of CAS (SD)	Change from Baseline to 90-day of CAS (SD)
Median						
95% Confidence Interval	(7.5, 7.9)	(7.1, 7.4)	(-0.6, -0.3)	(6.9, 7.3)	(6.7, 7.0)	(-0.4, -0.2)
HbA1c, %, Min, Max	5.9, 11.2	5.5, 9.3	-2.1, 1.1	6.0, 9.1	5.7, 9.2	-1.4, 0.5

Table 41 below summarizes time spent in Auto Mode and sensor usage from the start of subject use of the MiniMed 780G with Guardian 4 transmitter and Guardian 4 sensor during the CAS phase until the completion of 90-days of 780G use during the CAS phase. This data shows that subjects were in Auto Mode for greater than 90% of the time.

Table 41: Summary of Sensor Usage and Time Spent in Auto Mode, From Start of Auto-Mode use with the 780G system to 90-day visit of Continued Access Study Phase

Category	Percentage of Time	
	Subject 7-17 Years of Age	Subject 18-75 Years of Age
Time spent using sensor	93.7 %	94.1 %
Time spent not using sensor	6.3 %	5.9 %
Time spent in Auto Mode	94.4 %	95.1 %
Time spent in Manual Mode	5.6 %	4.9 %

The three tables below, Table 42, Table 43, and Table 44, show the results when subjects' pumps were programmed to setpoints of 100 mg/dL, 110 mg/dL and 120 mg/dL, while also programmed to different active insulin times (AITs) according to the subjects' needs. In subjects 7-17 years of age, the highest time in range (70-180 mg/dL) was observed with a setpoint of 110 mg/dL and the AIT programmed to 2-3 hours. In subjects 18-75 years of age, the highest time in range (70-180 mg/dL) was observed with a setpoint to 120 mg/dL and the AIT programmed to 2-3 hours.

Table 42: Glycemic Control Outcomes by Active Insulin Time, Setpoint 100 mg/dL, for 780G system use during the Continued Access Study Phase[*, #]*

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes
Number of Subjects	65	8	0	54	11	0

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes
Overall Average SG (mg/dL)	150.1 ± 14.1 (149.4)	161.1 ± 12.6 (156.2)	N/A	146.2 ± 13.2 (146.7)	155.7 ± 9.2 (158.4)	N/A
Overall SD SG (mg/dL)	55.9 ± 10.4 (55.1)	58.8 ± 7.2 (59.0)	N/A	47.8 ± 9.0 (47.9)	53.3 ± 5.1 (54.3)	N/A
Overall CV SG (%)	37.0 ± 4.4 (37.1)	36.6 ± 4.2 (36.5)	N/A	32.5 ± 4.1 (32.1)	34.2 ± 2.8 (33.9)	N/A
SG < 54 mg/dL (%)	0.5 ± 0.4 (0.3)	0.4 ± 0.4 (0.3)	N/A	0.3 ± 0.3 (0.2)	0.2 ± 0.2 (0.2)	N/A
SG < 70 mg/dL (%)	2.4 ± 1.6 (1.9)	1.9 ± 1.2 (1.7)	N/A	1.7 ± 1.2 (1.6)	1.3 ± 0.9 (1.2)	N/A
70-180 mg/dL (%)	72.7 ± 8.2 (73.3)	65.7 ± 8.2 (67.7)	N/A	77.0 ± 8.6 (77.8)	69.7 ± 5.5 (68.4)	N/A
SG > 180 mg/dL (%)	24.9 ± 8.5 (24.6)	32.4 ± 8.6 (29.2)	N/A	21.2 ± 9.0 (20.6)	29.0 ± 5.9 (30.6)	N/A
SG > 250 mg/dL (%)	6.7 ± 4.7 (5.6)	8.7 ± 4.5 (7.1)	N/A	4.1 ± 3.4 (3.3)	5.8 ± 2.4 (6.0)	N/A
*Values are presented by Mean ± SD (Median) except for number of subjects. # Subjects with at least 10 days' worth of CGM data in each AIT category and specific setpoint were included in analysis.						

Table 43: Glycemic Control Outcomes by Active Insulin Time, Setpoint 110 mg/dL, for 780G system use during the Continued Access Study Phase, #*

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes
Number of Subjects	26	3	1	7	0	0
Overall Average SG (mg/dL)	151.6 ± 10.1 (151.1)	181.6 ± 18.0 (185.6)	144.8 (144.8)	152.9 ± 19.5 (147.0)	N/A	N/A
Overall SD SG (mg/dL)	53.0 ± 10.3 (51.7)	68.7 ± 15.9 (64.8)	52.9 (52.9)	47.3 ± 12.9 (47.6)	N/A	N/A
Overall CV SG (%)	34.8 ± 5.1 (34.3)	37.5 ± 5.4 (34.9)	36.5 (36.5)	30.6 ± 4.8 (31.0)	N/A	N/A
SG < 54 mg/dL (%)	0.3 ± 0.4 (0.2)	0.3 ± 0.3 (0.1)	0.4 (0.4)	0.2 ± 0.2 (0.1)	N/A	N/A
SG < 70 mg/dL (%)	1.8 ± 1.3 (1.5)	1.1 ± 0.8 (0.8)	3.0 (3.0)	1.1 ± 0.7 (1.3)	N/A	N/A

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes
70-180 mg/dL (%)	73.5 ± 7.0 (73.2)	56.6 ± 10.4 (52.5)	73.7 (73.7)	74.5 ± 13.1 (75.5)	N/A	N/A
SG > 180 mg/dL (%)	24.7 ± 6.8 (25.0)	42.3 ± 10.0 (47.0)	23.3 (23.3)	24.4 ± 13.2 (23.2)	N/A	N/A
SG > 250 mg/dL (%)	6.0 ± 4.0 (5.1)	16.5 ± 8.7 (17.8)	4.0 (4.0)	5.0 ± 7.4 (3.3)	N/A	N/A
*Values are presented by Mean ± SD (Median) except for number of subjects. # Subjects with at least 10 days' worth of CGM data in each AIT category and specific setpoint were included in analysis.						

Table 44: Glycemic Control Outcomes by Active Insulin Time, Setpoint 120 mg/dL, for 780G system use during the Continued Access Study Phase, #*

Category	Subject 7-17 Years of Age			Subject 18-75 Years of Age		
	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes	AIT 120-180 minutes	AIT 195-240 minutes	AIT>240 minutes
Number of Subjects	24	2	0	6	1	0
Overall Average SG (mg/dL)	160.1 ± 14.1 (158.6)	163.2 ± 14.9 (163.2)	N/A	148.5 ± 4.2 (149.1)	171.3 (171.3)	N/A
Overall SD SG (mg/dL)	57.1 ± 8.5 (56.0)	56.8 ± 0.5 (56.8)	N/A	42.0 ± 5.4 (41.1)	61.0 (61.0)	N/A
Overall CV SG (%)	35.6 ± 3.7 (35.2)	35.0 ± 3.5 (35.0)	N/A	28.2 ± 3.1 (27.5)	35.6 (35.6)	N/A
SG < 54 mg/dL (%)	0.4 ± 0.5 (0.3)	0.5 ± 0.4 (0.5)	N/A	0.2 ± 0.2 (0.1)	0.2 (0.2)	N/A
SG < 70 mg/dL (%)	2.0 ± 1.5 (1.8)	2.3 ± 1.9 (2.3)	N/A	1.0 ± 0.6 (0.8)	1.1 (1.1)	N/A
70-180 mg/dL (%)	67.4 ± 8.1 (68.8)	62.8 ± 7.5 (62.8)	N/A	79.4 ± 5.6 (78.7)	58.7 (58.7)	N/A
SG > 180 mg/dL (%)	30.6 ± 8.6 (30.2)	34.9 ± 9.4 (34.9)	N/A	19.6 ± 5.1 (20.0)	40.2 (40.2)	N/A
SG > 250 mg/dL (%)	8.4 ± 5.0 (7.2)	8.7 ± 2.8 (8.7)	N/A	2.4 ± 1.4 (1.8)	11.8 (11.8)	N/A
*Values are presented by Mean ± SD (Median) except for number of subjects. # Subjects with at least 10 days' worth of CGM data in each AIT category and specific setpoint were included in analysis.						

Table 45 below provides the number of auto bolus events that occurred throughout the continued access study phase, glycemic control (i.e., average SG and percentage of SGs within various SG ranges) prior to and after auto bolus events, and the change in each category before and after auto bolus events. During the MiniMed 780G with Guardian 4 transmitter and Guardian 4 sensor CAS period, 67,152 automatic correction boluses were administered for 7–17-year-old subjects and 40,295 automatic correction boluses were administered for 18–75-year-old subjects. The percentage of SGs in the hypoglycemic range (<70 mg/dL) did not increase for either subject population. The data below show that the auto correction bolus feature in the MiniMed 780G is safe.

Table 45: Glycemic Control Prior to and After Auto Bolus Events, for 780G system use during the Continued Access Study Phase[*]

Category	Subject 7-17 Years of Age (N=109)			Subject 18-75 Years of Age (N=67)		
	2 hours prior event	**6 hours post event**	**Change from Prior to Post**	**2 hours prior event**	**6 hours post event**	**Change from Prior to Post**
Number of Auto Bolus Events	67152	67152	67152	40295	40295	40295
Sensor Glucose, Mean ± SD (95%CI)	154.5±9.8 (152.7,156.4)	161.1±10.7 (159.0, 163.1)	6.5±2.8 (6.0, 7.1)	151.5±11.6 (148.7,154.4)	156.3±11.7 (153.4,159.1)	4.7±2.5 (4.1, 5.3)
SG < 54 mg/dL (%)	0.3±0.3 (0.3, 0.4)	0.3±0.2 (0.2, 0.3)	-0.1±0.1 (-0.1, -0.1)	0.2±0.3 (0.2, 0.3)	0.2±0.2 (0.1, 0.2)	-0.1±0.1 (-0.1, -0.1)
SG < 60 mg/dL	0.7±0.6 (0.6, 0.8)	0.5±0.4 (0.4, 0.6)	-0.2±0.2 (-0.2, -0.1)	0.5±0.5 (0.4, 0.6)	0.3±0.3 (0.2, 0.4)	-0.2±0.2 (-0.2, -0.1)
SG < 70 mg/dL (%)	1.8±1.2 (1.6, 2.0)	1.3±0.9 (1.1, 1.5)	-0.5±0.4 (-0.6, -0.4)	1.4±1.2 (1.1, 1.7)	0.9±0.7 (0.7, 1.1)	-0.5±0.5 (-0.6, -0.4)
70-140 mg/dL (%)	43.7±7.4 (42.3, 45.1)	39.1±7.2 (37.8, 40.5)	-4.6±1.9 (-5.0, -4.2)	43.9±10.4 (41.4, 46.5)	40.4±10.0 (38.0, 42.8)	-3.5±2.2 (-4.1, -3.0)
70-180 mg/dL (%)	73.2±7.4 (71.8, 74.6)	69.4±8.0 (67.9, 71.0)	-3.7±1.6 (-4.0, -3.4)	77.3±8.9 (75.2, 79.5)	74.8±9.6 (72.5, 77.2)	-2.5±1.6 (-2.9, -2.1)
SG >140 mg/dL (%)	54.5±7.8 (53.0, 56.0)	59.6±7.4 (58.2, 61.0)	5.1±2.1 (4.7, 5.5)	54.7±11.0 (52.0, 57.4)	58.7±10.3 (56.2, 61.2)	4.0±2.4 (3.4, 4.6)
SG >180 mg/dL (%)	25.0±7.5 (23.6, 26.5)	29.3±8.1 (27.7, 30.8)	4.2±1.7 (3.9, 4.6)	21.3±9.2 (19.0, 23.5)	24.3±9.7 (21.9, 26.6)	3.0±1.6 (2.6, 3.4)
SG >250 mg/dL (%)	5.1±3.2 (4.5, 5.7)	6.6±3.9 (5.8, 7.3)	1.4±1.1 (1.2, 1.6)	3.3±2.9 (2.6, 4.0)	4.0±3.3 (3.2, 4.8)	0.8±0.8 (0.6, 1.0)
SG >350 mg/dL (%)	0.4±0.5 (0.3, 0.5)	0.5±0.7 (0.4, 0.6)	0.1±0.2 (0.0, 0.1)	0.2±0.3 (0.1, 0.3)	0.2±0.3 (0.1, 0.3)	0.0±0.1 (-0.0, 0.0)
*Values are presented by Mean ± SD (95% CI) except for number of bolus events						

Randomized Crossover Trial Comparing Automated Insulin Delivery with Predictive Low Glucose Suspend in People with Type 1 Diabetes[4]

The applicant conducted a prospective clinical study in New Zealand as a collaboration with Dr. Martin de Bock (Principal Investigator) and Christchurch Clinical Studies Trust Ltd. (Sponsor). The main purpose of this study was to compare the AHCL therapy (using the MiniMed 670G 4.0 insulin pump) with sensor augmented pump with predictive low glucose monitoring (SAP + PLGM) therapy in type 1 diabetes by comparing glycemic outcomes when the pump operated in Auto Mode versus Manual Mode.

This dual-center, randomized, open-label, two-sequence cross-over study in automated insulin delivery naïve participants enrolled 60 subjects aged 7-80 years with type 1 diabetes, and 59 of these subjects completed the study phases. Each study phase was 4 weeks, preceded by a 2-4-week run-in, and separated by 2-week washout.
Use of AHCL was associated with a statistically significant increase in the percentage of sensor glucose readings in the target range between 3.9 and 10.0 mmol/L (70 and 180 mg/dL) (70.4% versus 57.9%) relative to SAP + PLGM, meeting the predefined success criteria for clinical performance.

Treatment with AHCL was associated with a statistically significant decrease in percent of sensor glucose readings above 10.0 mmol/L (180 mg/dL) (27.5% versus 39.6%) relative to treatment with SAP + PLGM and a decrease in percent of sensor glucose readings less than 3.9 mmol/L (70 mg/dL) (2.1% versus 2.5%) relative to SAP + PLGM, meeting the predefined success criteria for safety.

There were no device-related serious adverse events during the AHCL treatment period and one possibly device related serious adverse event during the SAP + PLGM treatment period due to possible infusion set occlusion.

Patient/parent/guardian surveys showed greater technology satisfaction after use of AHCL relative to the surveys completed after use of the system in SAP + PLGM.

A comparison of two hybrid closed-loop systems in adolescents and young adults with type 1 diabetes (FLAIR): a multicenter, randomized, crossover trial[5]

The AHCL system (using the MiniMed 670G 4.0 insulin pump) was evaluated in the FLAIR Study, which was an investigator-initiated, NIH-sponsored study conducted in US, Germany, Slovenia, and Israel. The main purpose of this study was to compare the effectiveness and safety of the MiniMed 670G System with the MiniMed 670G 4.0 system.

This study was a randomized crossover trial with two 12-week crossover periods in auto mode preceded by a run-in phase. Enrollment was proceeded with the goal of at least 100 participants completing the crossover trial. A maximum of 124 individuals may be enrolled and start the run-in phase and a total of approximately 112 are

expected to enter the crossover trial.

The investigational AHCL system was found to induce a greater reduction in hyperglycemia during the day (the primary outcome) without an increase in hypoglycemia as compared to the MiniMed 670G system. The effects of the enhancements in the algorithm in the investigational AHCL system were evident in the greater time spent in Auto Mode than with the commercially approved MiniMed 670G system, resulting in an increase in the length of time per day that glucose concentrations were in the target range (70–180 mg/dL [3·9–10·0 mmol/L]). The modification of the algorithm was also evident in the way insulin was delivered, as indicated by a substantial shift in the basal to bolus ratio of insulin delivery from being approximately 1:1 with the MiniMed 670G system to 1:2 with the AHCL system, with just over a third of boluses delivered as automated-correction boluses.

Time in the target glucose range increased from 57% to 67% with use of the AHCL system compared with 57% to 63% with use of the MiniMed 670G system. The 4% difference in the increase in mean time spent in target range seen with the AHCL system compared with the MiniMed 670G system represents close to 1 hour per day with glucose levels in the target range. 65% of participants with the AHCL system exhibited an improvement of the time in range (70-180 mg/dL) of 5% or more, versus 53% of participants with the 670G system. Compared to the 670G system, time in the glucose range less than 54 mg/dL (<3.0 mmol/L) decreased from 0.50% to 0.46% (-0.04%; $p < 0.0001$) with use of the AHCL system.

Of the 112 participants, 7 adverse events were reported for 7 (6%) participants during use of the MiniMed 670G system and 6 events for 6 (5%) participants during use of the AHCL system. While using the AHCL system, severe hypoglycemia occurred in one participant who forgot to give a manual bolus for dinner and subsequently gave a bolus an hour after dinner followed by another bolus for a late-night snack 1–2 hours later. The participant recovered without sequelae. During use of the MiniMed 670G system, two participants had a serious adverse event that required hospitalization: one due to suicidal tendencies and one due to a ruptured appendix. None of these events were determined to be due to study treatment.

Real-World Performance of the MiniMed 780G System: Impact of Initiating Automated Basal and Correction Boluses

The applicant evaluated the outcomes associated with real-world use of the MiniMed 780G System with the GS3 in the EU (commercially available October 2020). The main purpose of this analysis was to evaluate the real-world performance of the MiniMed 780G System with Guardian Sensor (3) in individuals for CGM derived metrics and reduction in HbA1C or Glucose Management Indicator (GMI) compared to baseline (before automatic basal and correction boluses).

The analysis included 128 individuals who provided consent for analysis using the MiniMed 780G System with Guardian Sensor (3) that uploaded data voluntarily to the CareLink Personal database from October 5, 2020, to December 11, 2020. The mean

SG values, GMI, percentage of time spent in the various glycemic ranges, and time spent in Auto mode were determined for individuals having at least 10 days of SG data both before and after initiating automated basal and correction boluses.

The study showed a high percentage of time spent in Auto Mode (92.4%) with a mean sensor glucose of 144.8 mg/dL. Compared to baseline, there was a statistically significant increase in percentage of time spent in range (70–180 mg/dL) with AHCL (76.1% vs. 63.6%; p< 0.001) without an increase in hypoglycemia. Similarly, compared to baseline, there was a statistically significant increase in the percentage of individuals achieving a GMI <7.0% which increased by 41.4% (36.7% to 78.1%; p < 0.001) and the percentage of individuals achieving a TIR >70% which increased 39.1% (36.7% to 75.8%; p< 0.001) with AHCL. The data from real world evidence using MiniMed 780G supports the pivotal trial data by demonstrating robust improvement in all CGM derived glycemic metrics and GMI.

Real-World Performance of the MiniMed 780G System with Guardian 4 sensor: Initiating Automated Basal and Correction Boluses

The applicant evaluated the outcomes associated with real-world use of the MiniMed 780G System with the Guardian 4 sensor in the EU (commercially available October 2021). The main purpose of this analysis was to evaluate the real-world performance of the MiniMed 780G System with Guardian 4 sensor in individuals for CGM-derived metrics and Glucose Management Indicator (GMI).

The analysis included 3,662 individuals (1,107 were age 15 years and younger, 2,448 were older than 15 years of age and 107 did not report their age) using the MiniMed 780G System with Guardian 4 sensor who voluntarily uploaded data to the CareLink Personal database and who provided consent for the analysis of their data. The data used in the analysis were collected as of January 12, 2022. The mean SG values, GMI, percentage of time spent in the various glycemic ranges, and time spent in Auto mode were determined for individuals having at least 10 days of SG data.

The study showed that subjects ≤15 years of age spent 93.69% of time in Auto mode with a mean sensor glucose of 154.77 mg/dL, and subjects older than 15 years spent 93.43% of time spent in Auto mode with a mean sensor glucose of 151.39 mg/dL. Both subject groups spent greater than 70% of time spent in the target range (70-180 mg/dL) and less than 2% of time in the hypoglycemic range (<70 mg/dL), with an overall mean sensor glucose value of 152.43 mg/dL and overall GMI of 6.96%. The data from real world use of the MiniMed 780G system with Guardian 4 transmitter and Guardian 4 sensor are consistent with the results of the AHCL algorithm pivotal study results, therefore demonstrating that the MiniMed 780G system with Guardian 4 transmitter and Guardian 4 sensor is safe.

Transitioning of People with Type 1 Diabetes from Multiple Daily Injections and Self-Monitoring of Blood Glucose Directly to MiniMed 780G Advanced Hybrid Closed-Loop System: a two-center, randomized, controlled study[1]

The aim of this study was to evaluate the outcomes of transitioning to the MiniMed 780G advanced hybrid closed-loop (AHCL) system in adult individuals with type 1 diabetes mellitus (T1DM) naive to continuous subcutaneous insulin infusion (CSII) and continuous glucose monitoring (CGM) technologies. The results of this study were published in the Diabetes Care Journal: https://doi.org/10.2337/dc22-0470. This was a two-center, randomized, controlled, parallel-group trial with evaluation of individuals with T1DM aged 26–60 years managed with multiple daily injections (MDI) and self-monitoring of blood glucose (BGM) with HbA1c < 0.001). The time with levels below range (< 0.001). Participants from the AHCL group also had significant improvements in HbA1c levels (treatment effect 20.6% [95% CI 20.9, 20.2]; P = 0.005).

The primary and secondary glucose and clinical outcomes are provided in Table 46.

Table 46: Primary and Secondary Glucose and Clinical Outcomes

	Treatment arm (n=20)		**Control arm (n=17)**	
	Baseline	**MiniMed 780G system**	**Baseline**	**MDI + BGM**
HbA_{1c} (%; mmol/mol)	7.05 ± 0.8; 54 ± 9	6.7 ± 0.4; 50 ± 5	7.4 ± 1.2; 57 ± 13	7.4 ± 0.8; 57 ± 9
SG mg/dL	139.9 ± 21.2	133.2 ± 8.9	151.0 ± 23.6	153.1 ± 25.3
GMI (%)	6.66 ± 0.51	6.50 ± 0.21	6.92 ± 0.56	6.97 ± 0.61
CV of SG (%)	39.0 ± 7.1	30.6 ± 4.7	39.5 ± 4.7	40.7 ± 6.3
%SG < 54 mg/dL	2.9 ± 3.8	0.3 ± 0.4	2.7 ± 4.9	2.6 ± 3.9
%SG < 70 mg/dL	8.7 ± 7.3	2.1 ± 1.7	7.5 ± 7.9	8.1 ± 7.1
%SG 70-180 mg/dL	69.3 ± 12.3	85.0 ± 6.3	62.8 ± 10.7	61.5 ± 11.2
%SG >180 mg/dL	22.0 ± 12.3	12.9 ± 5.8	29.8 ± 13.4	30.5 ± 14.2
%SG >250 mg/dL	5.2 ± 6.4	1.6 ± 1.6	7.6 ± 5.8	9.3 ± 8.3
Body weight (kg)	76.3 ± 14.7	75.6 ± 16.5	77.7 ± 14.4	77.8 ± 15.3
BMI (kg/m^2)	24.5 ± 3.3	25.6 ± 2.6	25.6 ± 2.6	77.8 ± 15.3

Table 47 provides outcomes of the QoL-Q Diabetes Questionnaire.

Table 47*: Outcomes of the QoL-Q Diabetes Questionnaire*

	Treatment arm (n=20)		**Control arm (n=17)**	
	Baseline	**MiniMed 780G system**	**Baseline**	**MDI + BGM**
Overall QoL Score	187.2 ± 32	202.5 ± 54.2	173.87 ± 46.24	173.6 ± 53.34
Feeling well	7.9 ± 3.2	9.8 ± 3.1	6.73 ± 3.31	7.87 ± 3.38
Working	7.4 ± 2	10.4 ± 2.9	7.93 ± 4.15	7.33 ± 3.02
Eating as I would like	4.9 ± 2.7	7.1 ± 3.3	3.87 ± 1.88	4.07 ± 2.62
Doing “normal” things	7.6 ± 2.9	9.9 ± 3.7	8.33 ± 3.66	8.21 ± 3.85
Family relationships/ friendships	9.9 ± 3.4	10 ± 3.5	8.27 ± 3.13	10.2 ± 3.49
Going out or socializing	8.2 ± 2.7	8 ± 2.8	8.07 ± 3.43	9.33 ± 2.97
Partner/spouse relationship	9.8 ± 3	9.7 ± 4	9.53 ± 3.34	9.73 ± 4.1
Enjoying sexual activity	8.4 ± 2.3	8.8 ± 3.1	8.71 ± 2.43	9.21 ± 3.91
Being physically active	8 ± 2.1	8.8 ± 2.8	7.47 ± 3.14	8.36 ± 3.08
Feeling in control of my body	7.9 ± 2.5	8.7 ± 3.4	7.5 ± 2.44	8.93 ± 3.59
Looking good	7.2 ± 2.2	7.7 ± 2.5	7.79 ± 2.78	8.2 ± 3.38
Having holidays	8.9 ± 3.5	9.3 ± 3.4	6.93 ± 3.01	7.53 ± 2.59
Affording the things I would like	8.9 ± 3.5	8.9 ± 3.6	8.2 ± 3.47	8.07 ± 3.2

	Treatment arm (n=20)		Control arm (n=17)	
	Baseline	**MiniMed 780G system**	**Baseline**	**MDI + BGM**
Driving	8.6 ± 3.4	9.1 ± 3.2	7.8 ± 4.18	7.93 ± 3.79
Practicing my religion	8.4 ± 3.9	8.4 ± 3.8	7.18 ± 4.33	6.3 ± 3.92
Sleeping	8.6 ± 2.5	9.8 ± 3.3	7.27 ± 2.09	7.5 ± 4.31
Looking after or being useful to others	8.9 ± 2.2	8.7 ± 1.9	7.33 ± 2.47	7.31 ± 3.3
Pets/animals	7.7 ± 1.9	8.8 ± 3.7	7.09 ± 2.88	6.44 ± 2.35
Being independent	9.7 ± 3.2	11.1 ± 3.1	9.8 ± 2.93	9.62 ± 3.73
Being in control of my life	9.2 ± 3.2	10.6 ± 3.5	9.2 ± 3.21	8.57 ± 4.26
Being spontaneous	6.5 ± 2.7	6.5 ± 2.7	6.67 ± 3.62	6.67 ± 3.62
Being treated as "normal"	9 ± 2.9	9.3 ± 4.1	9.4 ± 3.14	9.36 ± 4.29
Having confidence	9 ± 2.2	9.3 ± 3.3	8.2 ± 3.21	8.29 ± 4.1

XII. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Clinical Chemistry and Clinical Toxicology Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The results of the clinical studies performed to support this submission establish a reasonable assurance of effectiveness that the MiniMed 780G system, with either

Guardian Sensor (3) or Guardian 4 sensor, can automatically adjust basal insulin rates and calculate and deliver auto correction boluses based on CGM values.

Additionally, a reasonable assurance has been demonstrated that the system can detect trends and track patterns and temporarily suspend and resume delivery of insulin when used as intended, as an adjunct to blood glucose testing, when used with Guardian Sensor (3) or Guardian 4 sensor, in subjects with type 1 diabetes mellitus.

The effectiveness of the Guardian 4 sensor component was based on the accuracy evaluation of sensor glucose values compared to the blood glucose values measured by the comparator method during in-clinic sessions spanning the wear period of the sensor (7 days). The performance data presented above established the sensor performance across the claimed measuring range (50 mg/dL to 400 mg/dL glucose), and the precision, with zero calibrations throughout the up to 7-day wear period for the Guardian 4 sensor. The performance data presented above also established the performance of the alarms and alerts of the Guardian 4 sensor.

The results of the clinical studies performed to support approval establish a reasonable assurance that the MiniMed 780G system with Guardian Sensor (3) and Guardian 4 Sensor are effective for their intended use.

B. Safety Conclusions

An understanding of the risks of the device are based on nonclinical laboratory data as well as on data collected in the clinical studies conducted to support PMA approval that are described above.

The following events are possible adverse device effects of inserting a sensor into your skin: local infection, inflammation, pain or discomfort, bleeding at the glucose sensor insertion site, bruising, itching, scarring or skin discoloration, hematoma, tape irritation, sensor or needle fracture during insertion, wear or removal.

Potential device related non serious events include:

- Skin Irritation or redness
- Infection
- Pain or discomfort
- Bruising
- Edema
- Rash
- Bleeding
- Induration of skin
- Allergic reaction to adhesives
- Hyperglycemia following inadequate or suspension of insulin delivery (which can result from catheter occlusion, hardware or software malfunction, or erroneous CGM readings)

- Ketosis following inadequate or suspension of insulin delivery (which can result from catheter occlusion, hardware or software malfunction, or erroneous CGM readings)
- Hypoglycemia resulting from insulin over-delivery (which can result from catheter occlusion, hardware or software malfunction, or erroneous CGM readings)

Sensor breakage with fragments retained under the skin is a potential adverse event related to use of the CGM component of the system, but this was not observed during these studies. Based on post-market experience with similar devices, the occurrence and severity of these events do not raise major concerns.

Infection at the insulin pump infusion set insertion site and sensor insertion site is a potential complication related to insertion of the CGM or the insulin pump infusion set. Based on post-market experience with similar devices, the occurrence and severity of these events are not expected to be different from other approved infusion sets and CGM devices, and so do not pose an unreasonable risk.

The CGM readings (together with blood glucose meter readings) are used by the system to determine automated insulin delivery, including insulin suspension and insulin dosing, and are the basis for alerts for hypoglycemia and hyperglycemia. The Guardian Sensor (3) readings are also to be used by the patient for tracking and trending, when in Manual Mode. While in manual mode, the Guardian Sensor (3) readings are intended to be used adjunctively (i.e., confirmatory blood glucose meter readings should be used for diabetes treatment decisions) for tracking and trending of blood sugars. While in manual mode, the Guardian 4 sensor readings are also intended to be used adjunctively.

The consequences of a false positive (falsely high) glucose reading on the continuous glucose meter would be potential over-delivery of insulin via automated insulin delivery, which has the potential to lead to severe hypoglycemia or even death. The consequences of a false negative (falsely low) glucose reading on the continuous glucose meter would be potential under-delivery of insulin, which has the potential to lead to severe hyperglycemia or DKA.

A confirmatory blood glucose meter reading has the potential to mitigate some of the risk of falsely high or falsely low glucose sensor readings, as the patient could choose to override the settings of the system in some cases (i.e., decline to take additional bolus of insulin as recommended by the system in setting of falsely high continuous glucose reading or exit Auto Mode).

The most common adverse event observed in the clinical studies was hyperglycemia following inadequate insulin delivery, insulin suspension, or due to potential catheter occlusion. However, there were no events of device related DKA. Further, based on post-market experience with similar devices, the reported higher incidence of severe hyperglycemia reported does not seem to translate into an increased

clinical risk of severe hyperglycemia and the results of the clinical studies performed and described in section IX and X above support a reasonable assurance that the MiniMed 780G system is safe for its intended use.

C. Benefit-Risk Determination

Summary of Benefits

780G System with Guardian 3 CGM (GS3):

With use of the 780G System (AHCL algorithm) with the Guardian 3 CGM as the glucose input, the pivotal clinical study (G190075) reported overall findings of improved CGM metrics compared to baseline - time in range (70-180 mg/dL), time below range and time above range, as well as lower HbA1c, compared to baseline. These trends were noted in both the adult (18 years of age and older) as well as the pediatric (7-17 years of age) population. The new automated functionalities of the 780G System present opportunity for benefits related to convenience. It is important to note that there are important study design limitations (including lack of a dedicated control group, as well as that CGM metrics are not currently validated as surrogate clinical outcomes), so although these findings are generally thought to be beneficial to patients, there is still residual uncertainty around the types and extent of the specific clinical benefits that can be expected with use of the 780G System, and particularly around the new automated functionalities associated with the AHCL algorithm.

780G System with Guardian 4 CGM (G4S):

The 780G + G4S system was added to the continued access study once it was already underway with the 780G + GS3 configuration. Therefore, there was no data available within the pivotal study from subjects who were naive to the 780G system before using it with the G4S. There were no events of DKA that were device related during the continued access study in non-naïve AHCL users in this configuration, and the CGM metrics for the 780G + G4S system was comparable to that of the System with GS3. However, the transition in CGM sensor during the pivotal study limited the clinical data for the 780G + G4S system, particularly for AHCL naïve users. The sponsor provided real-world evidence (RWE) which included both AHCL nai"ve users (adults age >15 and pediatrics age :S 15) whose first experience was with the 780G system + G4S and non-nai"ve users (adults age >15 and pediatrics age :S 15) who transitioned from the GS3 to the G4S while using the 780G system and thus had experience with the AHCL prior to beginning the use of the G4S CGM as part of the system. The sponsor provided a comparison of the study groups and reported that the RWE was clinically comparable between the naïve and non-naïve AHCL + G4S users and non-naïve AHCL users, for both pediatric and adult users. The sponsor reported demographics and CGM metrics including mean CGM glucose, % time-in-range of 70-180 mg/dL, % time <54 mg/dL and % time <70 mg/dL in naïve vs non-naïve users of the 780G + G4S that was comparable between the two groups.

Summary of Risks

The pivotal study to evaluate safety and performance of the System did not have a dedicated control group. Rather, the data obtained from the clinical study was compared to the data from the same subjects prior to the run-in phase. Therefore, there is residual uncertainty due to the study design (lack of control group) about the risks of the device.
During the 3-month phase of the AHCL pivotal clinical study (and the continuation phase of the pivotal study):

- There were no reports of unanticipated serious adverse device effects.
- There were no device related adverse events.
- There were no reports of unanticipated non-serious adverse device/procedural effects.
- There were no reports of diabetic ketoacidosis events.
- There was one report of severe hypoglycemia (not device-related).

780G System with Guardian Sensor 3 CGM:

Although use of the 780G System's Auto Mode with the GS3 was associated with reduced exposure to high sensor glucose values (compared with the run-in phase) during the pivotal study, a higher incidence of severe hyperglycemia was reported in the 7- to 13-year age group during the pivotal study as compared with the 14 years and above age group. It is possible that the 7- to 13-year age group could have a higher risk of severe hyperglycemia compared to the 14 years and above population. However, the majority of the severe hyperglycemia episodes reported were related to potential occlusions. Given that there were no events of DKA that were device related during the AHCL study, as well as that sensor performance data during the AHCL study (compared to run-in) reported decreased sensor glucose time >180 mg/dL, >250 mg/dL, and > 350 mg/dL, the reported higher incidence of severe hyperglycemia reported does not seem to translate into an increased clinical risk of severe hyperglycemia.

780G System with Guardian 4 CGM:

In addition to the risks identified for the 780G System with GS3, based on the sensor accuracy data for the G4S, it is possible that the reported alert performance for the low sensor glucose ranges in the clinical study could result in an increased risk of hypoglycemia. However, there was no report of device-related of severe hypoglycemia in the study for the G4S configuration.

Further, the 780G System with the G4S configuration was added to the pivotal study once it was already underway with the 780G System with the GS3 configuration and thus only included experienced AHCL users. For this reason, there is residual

uncertainty about the performance of the 780G system with the G4S in AHCL naïve users.

Unlike the 670G and 770G systems, the 780G system is indicated down to 7 years old. Further, the 780G system with the G4S has a single sensor insertion site in the arm for all users whereas the GS3, which is already marketed, has different indications for the sensor insertion site(s). Given the changes between prior AHCL systems and the 2 CGMs compatible with the 780G system, user confusion or error may result in off-label use.

Patient Perspectives

Patient perspectives considered during the review included:

Patients want a variety of devices that provide information and aid in management of their glucose control to inform decision maintaining with their health care providers on lifestyle changes and treatment decisions. Patients have also expressed in conversations with FDA staff, on social media outlets, and at patient centered public conferences that they want devices that provide features that enable automated insulin delivery and are willing to accept reasonable risks related to such devices. This information was gathered via email, during patient-oriented conferences and face-to-face meetings with patients.

D. Overall Conclusions

The data in this application support a reasonable assurance of safety and effectiveness for this device when used in accordance with the indications for use. The benefits of using the MiniMed 780G system, as discussed above, outweigh the risks.

XIV. CDRH DECISION

CDRH issued an approval order on 4/21/2023. The final conditions of approval cited in the approval order are described below.

1. The MiniMed 780G Post Approval Study is a new enrollment study intended to collect additional information regarding safety of the 780G system following FDA approval and commercial launch of the system within the United States (US). Information collected will include insulin delivery and glycemic control information based on data uploaded from the pump and sensor in Auto Mode, as well as adverse events, device deficiencies, and glycosylated hemoglobin (A1C) levels reported by the pump user or their parent or guardian. Your PAS program will utilize the 780G pump's Bluetooth technology that automatically uploads device data to a cloud server via the user's phone when the patient is using a compatible device. Patients must agree to the automatic uploads and have internet connectivity to participate in the study. In addition, a survey will be sent to participants (or their parents or adult guardians) every month (e.g., via an application on

their phone) to collect information on adverse events, A1C and device deficiencies. You have proposed a minimum of 2,000 US participants, ages 7 and older, and to continue the program until at least one year of follow up data has been collected for study subjects. You anticipate the program to last approximately 24 months from enrollment of the first individual.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

[1] Matejko B, Juza A, Kiec-Wilk B, Cyranka K, Krzyzowska S, Chen X, Cohen 0, Da Silva J, Malecki MT, Klupa T. Transitioning of People With Type 1 Diabetes From Multiple Daily Injections and Self-Monitoring of Blood Glucose Directly to MiniMed 780G Advanced Hybrid Closed-Loop System: A Two-Center, Randomized, Controlled Study. Diabetes Care. 2022 Nov 1;45(11):2628-2635. doi: 10.2337/dc22-0470.