SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Automated Insulin Dosing Device System, Single Hormone

System Device Trade Name: MiniMed 670G System

Device Procode: OZP

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

Date(s) of Panel Recommendation: Not applicable

Premarket Approval Application (PMA) Number: P160017/S031

Date of FDA Notice of Approval: June 21, 2018

Breakthrough Device: Granted breakthrough device status (formerly known as the Expedited Access Pathway, or EAP) on June 21, 2018 because the Medtronic MiniMed 670 System will provide more effective management of type 1 diabetes, an irreversibly debilitating disease.

The 670G System was previously approved for use in ages 14 years and up and was approved on September 28, 2016. The SSED for the original approval (P160017) can be found on the CDRH website. The current supplement was to expand the indications for the device to include a user population of 7 to 13 years of age.

II. INDICATIONS FOR USE

MiniMed 670G System

The Medtronic MiniMed 670G system is intended for continuous delivery of basal insulin (at user selectable rates) and administration of insulin boluses (in user selectable amounts) for the management of Type 1 diabetes mellitus in persons, seven years of age and older, requiring insulin as well as for the continuous monitoring and trending of glucose levels in the fluid under the skin. The MiniMed 670G System includes SmartGuard technology, which can be programmed to automatically adjust delivery of basal insulin based on Continuous Glucose Monitor sensor glucose values, and can suspend delivery of insulin when the sensor glucose value falls below or is predicted to fall below predefined threshold values.

The Medtronic MiniMed 670G System consists of the following devices:
MiniMed 670G insulin pump, the Guardian Link (3) Transmitter, the Guardian Sensor (3), One-Press Serter, and the Contour NEXT Link 2.4 Glucose Meter. The system requires a prescription.

The Guardian Sensor (3) glucose values are not intended to be used directly for making therapy adjustments, but rather to provide an indication of when a finger stick may be required. All therapy adjustments should be based on measurements obtained using a home glucose monitor

and not on values provided by the Guardian Sensor (3).

Guardian Sensor (3)

The Guardian Sensor (3) is intended for use with the MiniMed™ 670G system to continuously monitor glucose levels in persons with diabetes. It is intended to be used for detecting trends and tracking patterns, and to be used by theMiniMed 670G system to automatically adjust basal insulin levels. It is indicated for use as an adjunctive device to complement, not replace, information obtained from standard blood glucose monitoring devices. The sensor is intended for single use and requires a prescription. The Guardian Sensor (3) is indicated for 7 days of continuous use.

One-press Serter

The One-press 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 670G System. The Guardian Link (3) Transmitter powers the glucose sensor, collects and calculates sensor data, and wirelessly sends the data to the MiniMed 670G insulin pump. The Transmitter is intended for single-patient multi-use.

Contour NEXT Link 2.4 Glucose Meter

The Contour Next Link 2.4 Wireless Blood Glucose Monitoring System is an over the counter (OTC) device utilized by persons with diabetes in home settings for the measurement of glucose in whole blood, and is for single patient use only and should not be shared. The Contour Next Link 2.4 wireless blood glucose monitoring system is indicatedfor use with fresh capillary whole blood samples drawn from the fingertip and palm only.
The Contour NEXT Test Strips are intended for self-testing by persons with diabetes for the quantitative measurement of glucose in whole blood samples from 20 to 600 mg/dL. The Contour Next Link 2.4 wireless blood glucose monitoring system is intended to be used to transmit glucose values to the MiniMed 670G pump and facilitate transfer of information to Medtronic CareLink Software through the use of radio frequency communication. The Contour Next Link 2.4 Wireless Blood Glucose Monitoring System is not intended for the diagnosis of, or screening for, diabetes mellitus. It is not intended for use on neonates.

III. CONTRAINDICATIONS

A prominent boxed warning is included in the labeling regarding use of the device in subjects under the age of 7 years as follows:

"Medtronic performed an evaluation of the 670G closed loop system and determinedthat it may not be safe for use in children under the age of 7 because of the way that the system is designed and the daily insulin requirements. Therefore this device shouldnot be used in anyone under the age of 7 years old. This device should also not be used in patients who require less than a total daily insulin dose of 8 units per day because the device requires a minimum of 8 units per day to operate safely."

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

- Insulin pump therapy is not recommended for people who are unwilling or unable to perform a minimum of four blood glucose tests per day. As insulin pumps use rapid acting insulin only, blood glucose 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.
- Pump therapy is not recommended for people whose vision or hearing does not allow recognition of pump signals and alarms.
- Do not use serter on products other than the Enlite Sensor (P120010) or Guardian Sensor (3). Medtronic cannot guarantee the safety or efficacy of this product if used with other products.
- 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 or the infusion of blood or blood products.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the MiniMed 670G System User Guide labeling.

V. DEVICE DESCRIPTION

There is no physical change to the MiniMed 670G System, previously approved under P160017, as a result of this panel track supplement. This current panel track supplement supports the expansion of the indicated population to include 7-13 year old people with type 1 diabetes.

The MiniMed 670G system is comprised of the following devices:

MiniMed 670G Pump (MMT-1780)

The MiniMed 670G pump (model MMT-1780) 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 determined basal rate profiles and user selected bolus amounts of insulin into the subcutaneous tissue through an infusion set.

The MiniMed 670G pump is offered in one model (MMT-1780). 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. It is intended to deliver insulin through a diffusion mechanism. Model MMT-1780 is compatible with a 3.0 mL reservoir. The pump only displays blood glucose level units in mg/dL and cannot be reconfigured by the user.
In addition to its delivery of insulin, the MiniMed 670G pump is designed to receive and display real-time interstitial fluid glucose values via the Guardian Link (3) Transmitter. When used in combination with Guardian Sensor (3), the transmitter sends sensor signals to the MiniMed 670G pump via radiofrequency (RF) telemetry. The 670G Pump has the following features and capabilities:

- Provides predictive sensor glucose alerts when sensor glucose values are high or low (please see 'Manual Mode' section below for details).
- Can receive blood glucose values from the Contour NEXT Link 2.4 Meter to use for sensor calibration.
- The pump can display Guardian Sensor (3) glucose values in real-time, and also store those values (and blood-glucose values from the meter) into its pump memory.
- "SmartGuard" Technology: There are two levels of this technology; the first is available in Manual Mode and the second in Auto Mode.
    - The first level of SmartGuard technology is available in Manual Mode:
        - This technology automatically suspends insulin when the sensor reaches a preset low limit (referred to as 'Suspend on Low')
        - This technology automatically suspends insulin when the sensor glucose value is predicted, using a proprietary predictive suspend algorithm, to reach a pre-set low limit, i.e., suspends before the low limit is reached (referred to as 'Suspend before Low').
        - When a Suspend event occurs, the user can choose to continue to keep insulin suspended, or the user can choose to resume insulin delivery.
        - Following a Suspend event, insulin delivery will automatically resume when the sensor glucose levels rise above the pre-set suspend threshold.
        - The 'Suspend on low' and 'Suspend before low' features are optional features available when the system is in Manual Mode.
        - This technology (in Manual Mode) provides a bolus calculator called the 'Bolus Wizard' that uses your settings to calculate an estimated bolus amount based on the meter blood glucose values and carbohydrates that the user enters. These settings should be set up with the help of a Health Care Practitioner before using the Bolus Wizard. Those settings include:
            - Carbohydrate Ratio
            - Insulin Sensitivity Factor
            - Blood Glucose Target
            - Active Insulin Time

    - The second level of SmartGuard technology is available in Auto Mode:
        - This technology automatically adjusts basal insulin delivery using continuous glucose monitor data, referred to as Auto Mode.
        - The Auto Mode feature can automatically increase or decrease the amount of insulin delivered based on sensor glucose values.

During Auto Mode operation, the user must manually deliver meal boluses that they calculate using the estimated amount of carbohydrates for meals at the time they are eaten. The user must also use the Auto Mode bolus feature to calculate boluses while in Auto Mode.

The MiniMed 670G Insulin Pump is designed to receive and display real-time glucose values received from the Guardian Link (3) transmitter. Guardian sensor (3) signals are

transmitted from the transmitter to the MiniMed 670G Insulin Pump via RF telemetry and converted into glucose concentrations based on calibration values from the Contour Next Link 2.4 meter. Signals are updated and transmitted to the pump every five minutes.

The real time sensor glucose values, displayed by the MiniMed 670G Insulin Pump, are not intended to be used directly for making therapy adjustments. The user can use the tracking and trending of sensor glucose values to help determine if an unplanned finger stick measurement may be needed. In addition, sensor glucose values should not be used to modify insulin therapy. All manual insulin therapy adjustments should be based on measurements obtained using a blood glucose meter and not based on the sensor glucose value displayed by the MiniMed 670G Insulin Pump.

Manual Mode

The user can set the pump to temporarily suspend insulin delivery automatically when the sensor glucose level is equal to or less than a selected threshold. The user has the capability to select a 'Suspend on Low' threshold within the 50 mg/dL to 90 mg/dL range. When the 'Suspend on Low' tool is set to 'ON', the system compares the sensor glucose value and the programmed Suspend threshold whenever the sensor glucose value is updated (every five minutes). If the sensor glucose value falls below the set threshold, insulin delivery will be suspended. Once the sensor glucose rises above that set threshold, insulin delivery will resume. The use of the 'Suspend on Low' tool is optional and the user can turn the tool 'ON' and 'OFF'.

The pump also includes the new Predictive Low Management tool that allows the user to set a glucose value threshold where the pump will suspend the insulin delivery if the blood glucose value is predicted to reach the selected threshold in the near future ('Suspend before Low'). The user can set their low sensor glucose threshold value from 50 mg/dL to 90 mg/dL; insulin delivery will suspend when the sensor glucose value is predicted to reach or fall below a level that is 20 mg/dL above the set low limit threshold value within approximately 30 minutes. The user has the ability to program the length of time in which suspension will occur pending the blood glucose threshold 30 minutes before the threshold is reached. Once the sensor glucose rises above that set threshold, insulin delivery will resume. The use of the 'Suspend on Low' tool is optional and the user can turn the tool 'ON' and 'OFF'.

When the sensor glucose value is below or predicted to be below the set threshold, an alarm and siren occurs and the pump suspends, and the user may elect to continue the suspend, or cancel the temporary pump suspension of insulin delivery at any time.

If the user does not respond to the 'suspend on low' or 'suspend before low' alarm or siren, the pump will automatically suspend for up to two hours.

If the user cancels the suspension of insulin delivery, the system will continue to deliver insulin at the programmed basal rate until the next time the sensor glucose value is below the set threshold value. The alarm and siren will then re-sound, and the pump will suspend (unless canceled by the user).

If the user responds to the alarm or siren by electing to accept the insulin suspension, the pump will suspend for at least 30 minutes and up to a maximum of 2 hours; the pump may resume insulin delivery if the sensor glucose value rises above the set low threshold after 30 minutes have passed and before or up to the 2 hours maximum suspension time. The user can manually

resume insulin at any time. At the end of the two-hour maximum, the pump will resume insulin delivery until the next sensor glucose value is below the set threshold suspend value.

The user can cancel the temporary pump suspension at any time during the two-hour period regardless if the suspension occurred because the user was not able to respond to the initial alarm or he/she accepted the suspension. The pump may also resume insulin delivery on its own based on sensor glucose values or predicted sensor glucose values (if the sensor glucose value indicates that the user has recovered from the set threshold low glucose value). The table below summarizes the suspend features.

Table 1: Suspend on Low and Suspend before Low Feature and Related Resumption Options

	Suspend Features	
What Happens	**Suspend on Low**	**Suspend before Low**
The pump suspends insulin delivery	The predetermined sensor blood glucose threshold is reached.	The predetermined sensor blood glucose threshold is predicted to be reached within 5 to 30 minutes (time period predetermined by
The user accepts the pump suspension	The pump will suspend for at least 30 minutes and up to a maximum of 2 hours.	The pump will suspend for at least 30 minutes and up to a maximum of 2 hrs.
The user responds to the insulin suspend and the system suspends insulin for two hours (maximum suspension time)	If insulin was suspended for two hours, then at the end of the two-hour maximum, the pump will resume insulin delivery. The pump will not suspend insulin again until after the refractory period* and the next sensor glucose value is below the set low glucose suspend value.	If insulin was suspended for two hours, then at the end of the two-hour maximum, the pump will resume insulin delivery. The pump will not suspend insulin again until after the refractory period* and the next sensor glucose value is predicted to go below the set low glucose suspend value.
The user cancels suspension	The system will resume insulin delivery at the programmed basal rate until the next time the sensor glucose value is below the set threshold value.	The system will resume insulin delivery at the programmed basal rate until the next time the sensor glucose value is below the set threshold value.
The user does not respond to the suspend alert	The pump will automatically suspend for up to two hours if the sensor glucose does not detect that the user's glucose values are or are predicted to go above the low glucose level.	The pump will automatically suspend for up to two hours if the sensor glucose does not detect that the user's glucose values are or are predicted to go above the low glucose level.

	Suspend Features	
What Happens	**Suspend on Low**	**Suspend before Low**
The sensor glucose a glucose value above low glucose pre-set level	Pump may resume insulin delivery on its own after 30 minutes based on sensor glucose values glucose values.	Pump may resume insulin delivery on its own after 30 minutes based on sensor glucose values or predicted sensor glucose values.

* After a Suspend event occurs, there is a period of time when the suspend functionality is unavailable (refractory period). This time will vary depending on whether or not the user responds to the Suspend event. Please see the labeling for the MiniMed 670G System regarding how the suspend functions work. The user can manually suspend insulin delivery at any time.

The MiniMed 670G Insulin Pump is capable of storing 90 days of pump history and glucose sensor data. The pump has a graphical display that the user can use to view the glucose history for the past 3, 6, 12 and 24 hours, high/low glucose alarms and display of retrospective glucose trend information.

Stored pump history and glucose data can be downloaded to a personal computer for review and analysis, to track patterns and improve diabetes management. Data is downloaded from the pump to CareLink therapy management software.

The MiniMed 670G pump is compatible with commercially available Medtronic Paradigm infusion sets and their 3 mL volume reservoirs. It was not necessary to develop new infusion sets or reservoirs for use with this pump.

Auto Mode

The MiniMed 670G Insulin Pump contains an Auto Mode feature; this new tool uses an algorithm to automatically adjust basal insulin delivery using continuous glucose monitor data. When in Auto Mode, the pump responds to fluctuations in interstitial fluid glucose levels measured by the continuous glucose monitor; the Auto Mode feature can automatically increase or decrease the amount of basal insulin delivered based on sensor glucose values.

Auto Mode does not administer meal boluses. During Auto Mode operation, users must deliver meal boluses by entering the amount of insulin they want to deliver based on the estimated amount of carbohydrates they are eating. Failure to deliver meal boluses in association with meals during Auto mode operation can result in significant post meal hyperglycemia.

The Auto Mode algorithm is designed to adjust the user's basal insulin rates to try to keep them at a target blood glucose level. The standard target glucose setting in Auto Mode is 120 mg/dL, and the target can also be set temporarily to 150 mg/dL for exercise and other events. In addition, blood glucose readings above 150 mg/dL will prompt the Auto Mode feature to calculate if a correction bolus is needed; if needed, a correction bolus will be recommended to the users, who can choose whether they want to deliver that correction

bolus. Users should check their blood glucose levels using a blood glucose meter before administering a correction bolus.

When first using the device, Auto Mode cannot be activated until the system completes a 48-hour warm-up period while the user uses the pump in manual mode to deliver insulin. In addition, before activation, the user must cancel any temporary basal rates, ensure delivery is not suspended, set a carbohydrate ratio, set high and low glucose settings, and enter a blood glucose value obtained by using a blood glucose meter if one has not been entered in the last 12 minutes. Carbohydrate ratios and high and low glucose settings should be discussed and established with the user's healthcare practitioner before use of Auto Mode begins.

There is an additional feature, called the Safe Basal feature, which will be activated in Auto Mode when the system encounters specific issues that the user should address; the user cannot manually enable Safe Basal as it is a mandatory automatic feature that activates when the pump encounters these types of issues. This feature is designed to be a safety net when in Auto Mode. The pump will transition into Safe Basal if the system detects the user is getting too little or too much basal insulin, if the pump detects an issue with the sensor or a discrepancy between blood glucose meter and sensor glucose readings, or if the pump has not received sensor glucose values in over 5 minutes. When the pump encounters an issue, it transitions to Safe Basal; in Safe Basal, the pump supplements the user's basal insulin needs by delivering a steady state basal rate, which allows the user time to perform the additional actions prompted by the pump that are required to ensure Auto Mode stays active. Safe Basal does not automatically adjust basal insulin and instead delivers a steady basal rate until the user has addressed the issue that triggered the pump to activate Safe Basal. After 90 minutes in Safe Basal, if the condition(s) that caused the pump to transition into Safe Basal have not been resolved, the pump will automatically exit Auto Mode and enter Manual Mode. If Auto Mode is active, then the 'Suspend on Low' and 'Suspend before Low' features from the 'Manual Mode' are unavailable and inactive. However, while in Auto Mode, basal insulin is adjusted by decreasing or suspending automatically based on continuous glucose monitor sensor values if the user is experiencing low glucose. The table below describes the available features and accessibility within each mode (Auto Mode and Manual Mode).
Note that, although Safe Basal is not mentioned in the table below, it is only available in Auto Mode and cannot be activated by the user, as it is a mandatory automatic feature that activates when the pump encounters an issue that the user should address (see description above).

Table 2: Modes and Related Accessibility

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.	This is the default mode and the user does not have to specifically turn this mode on.	There is a mandatory severe low alarm at 50 mg/dL; 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?
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 at 50 mg/dL 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 before Low is turned on.	There is a mandatory severe low alarm at 50 mg/dL 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 user has to turn this mode on and certain pre-defined conditions have to be met.	There is a mandatory severe low alarm at 50 mg/dL; The user can also set optional high and low alerts to sound on or before set sensor glucose levels.

Guardian Link (3) Transmitter System (MMT-7811)

The Guardian Link (3) Transmitter System consists of the Guardian Link (3) Transmitter (MMT-7811), the Charger (model MMT-7715), and the Tester (model MMT-7736).

The Guardian Link (3) Transmitter interfaces directly with the glucose-sensor assembly. The Guardian Link (3) Transmitter provides power to the glucose sensor, and measures the sensor signal current from the glucose sensor.

The sensor signal current is an electrical current level that is proportional to the glucose level in the user's subcutaneous interstitial fluid. The sensor signal current is converted to a digital signal, which is filtered to reduce noise artifacts. This digital signal is sent to the MiniMed 670G pump every 5 minutes, using radio frequency (RF).

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, when inserted in the user's abdomen (or in the abdomen or the buttock for users 7-13 years old) 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 670G Pump.

When making treatment decisions, such as determining insulin dose for meals, the MiniMed

670G continuous glucose monitor (CGM) values should not be used, as they are not intended to be used to make such treatment decisions. The MiniMed 670G continuous glucose monitor does not 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.

Users should calibrate the Guardian Sensor (3) at least every 12 hours using meter blood glucose values. Calibration is necessary for sensor function, and more frequent calibration can help to increase the accuracy of the sensor. The system requires a minimum of two calibrations per day, and four calibrations per day are recommended. The system is contraindicated for patients unwilling or unable to do frequent blood glucose meter measurements.

If the user obtains blood glucose values using the Contour Next Link 2.4 Meter, the user may transmit blood glucose values via radiofrequency to the MiniMed 670G pump to be used for sensor calibrations. If the user uses a different FDA cleared blood glucose meter to calibrate the Guardian Sensor (3), the user must manually input the blood glucose values into the pump to be used for sensor calibration. Additionally, users who use the Contour Next Link 2.4 should calibrate with values obtained using fingersticks; users should not use readings obtained from blood from alternative sites (e.g. palm).

One-Press Serter

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

Contour Next Link 2.4 Meter (MMT-1352 and MMT-1152) and Test Strips

The Contour Next Link 2.4 Meter can be used with the MiniMed 670G system; the meter wirelessly sends blood glucose values to the insulin pump for sensor calibration via radiofrequency. The meter was also previously cleared under K110894. Specifications and performance requirements were established for the meter and evaluated as part of the class III MiniMed 670G System. The sponsor verified and validated the specifications and performance requirements of the meter for the MiniMed 670G System. The sponsor provided blood glucose meter specifications, rationale for requirements for the meter, and impact of error on the sensor, predictive low alerts, threshold glucose suspend, and the predictive low glucose management and hybrid closed loop features in the original PMA submission. The sponsor carried out error impact analysis in order to determine the lot release criteria for the meter test strips. Based on the information provided in the original PMA submission, P160017, the meter specifications meet the clinical needs of the MiniMed 670G system.

Additional System Devices

The following additional accessory devices are compatible with the MiniMed 670G Insulin Pump:

Table 3: Additional System 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-369, MMT-370, 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-886
Paradigm Reservoir	MMT-332A
Optional Devices	**Model Numbers**
CareLink USB 2.4	MMT-7306
CareLink Online (Personal)	MMT-7333
CareLink Pro	MMT-7335

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Control of diabetes can be achieved through a combination of various behaviors and methods.

Self-behaviors include healthy eating, taking the clinically indicated medications, and being active. Persons with diabetes may also administer insulin by injection or using other insulin infusion pumps as prescribed by their physician. An insulin pump is an alternative to multiple daily insulin injections (via insulin syringe or an insulin pen). Periodic self-glucose monitoring using home use blood glucose meters provides information regarding variations in glucose levels.

Methods of monitoring glycemic control include periodic measurement of Hemoglobin A1c (HbA1c) which reflects blood glucose control over a three-month period. Self-monitoring of blood glucose using glucose meters and test strips provides quantitative measurements of blood glucose at a single point in time for users and their healthcare providers. This helps to monitor the effectiveness of glycemic control, as well as make more immediate treatment modifications.

Currently, cleared or approved insulin infusion pumps may be used for continuous subcutaneous insulin infusion. Additionally, commercially available sensor-augmented insulin infusion pumps or continuous glucose monitoring systems may be used to record continuous interstitial glucose information and provide real-time hypoglycemia and hyperglycemia alerts.

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

VII. MARKETING HISTORY

The MiniMed 670G System was approved for marketing in the United States in September 2016. The device has not been withdrawn from the market for any reason related to its safety or effectiveness.

The insulin reservoirs and infusion sets used with the 670G System are also the same as those currently used with the MiniMed 530G System (P120010) and the MiniMed 630G System (P150001). These devices have not been withdrawn from commercial distribution for any reason, related to either safety or effectiveness.

VIII. PROBABLE 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 adhesives

Sensor breakage with fragments retained under the skin is a potential adverse event related to use of the CGM component of the 670G system, but this was not observed during these studies. Based on post-market experience with similar devices and the results observed in these clinical studies, 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 these clinical studies, the occurrence and severity of these events are not expected to be different from other approved infusion sets and CGM devices.

Use of insulin pumps are 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 670G device as intended could harm themselves. Therefore, the device is for prescription use only and contraindicated for people unwilling or unable to perform a minimum of four fingerstick blood glucose meter tests per day 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 the 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 the 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 670G System. 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 the suspension/reduction of insulin delivery.

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 670G system. 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 reading on the continuous glucose monitor 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 reading 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

The MiniMed 670G System remains unchanged as a result of this panel track supplement, though the indicated population has been expanded to include 7 to 13 year old people with type 1 diabetes. However, a human factors study of use of the MiniMed 670G System by a pediatric population ages 7-13 was conducted. A summary of this human factors study is provided below. Please refer to the Summary of Safety and Effectiveness Data (SSED) for the original PMA, P160017, for other pre-clinical/laboratory studies that supported the approval of the MiniMed 670G System and its components.

Human Factors Testing

Medtronic conducted a usability validation study to evaluate the MiniMed 670G System, with continuous glucose monitoring and auto mode (HCL) function, to provide evidence that younger children (7 to 13 years of age) diagnosed with T1DM can, under the supervision of a caregiver, safely and effectively use the MiniMed 670G System.

Thirty users representing both pediatric novice and pediatric experienced patients and their caregivers participated in the usability validation study. These representative users performed critical tasks associated with using the MiniMed 670G system in both Manual and Auto Modes with the continuous glucose monitoring system. Task Analysis was used to determine critical tasks. Two representative user groups were studied (15 per group):

- Pediatric Novice Insulin Pump Users (ages 7-13 years)
  - Users in this group were not currently external pump users, had less than 6 months of experience with a Medtronic pump, or were currently using a competitor pump.
- Pediatric Experienced Insulin Pump Users (ages 7-13 years)
  - Users in this group currently were using a Medtronic external insulin pump for more than 6 months.

All use difficulties and close calls observed during completion of critical tasks were analyzed, and the root causes and impacts were assessed. For any close calls, a residual risk analysis was performed to determine whether design changes would further reduce the risks and to assess the residual risks related to the benefits to the patient.

The Human Factors usability validation study demonstrated that the MiniMed 670G System, with continuous glucose monitoring and auto mode (hybrid closed loop (HCL)) function, is safe and effective for use by patients with T1DM 7 to 13 years of age with assistance from their adult caregivers.

B. Animal Studies

None.

C. Additional Studies

None

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The original approval of P160017 was based on three pivotal studies to establish a reasonable assurance of safety and effectiveness of the MiniMed 670G System for its intended use, including the accuracy performance of the Guardian Sensor (3) in people 14 and older. Please refer to the Summary of Safety and Effectiveness Data (SSED) for the original PMA, P160017, for details on those studies.

Medtronic performed clinical studies to establish a reasonable assurance of safety and effectiveness of the 670G System in pediatric subjects ages 7-13 years. A summary of the clinical studies is presented below.

Table 4: Summary of P160017/S031 Clinical Studies

Clinical Study	Patient Population	Study Design/Objective
Safety Evaluation of the Hybrid Closed Loop (HCL) System in Pediatric Subjects with Type 1 Diabetes (described in Sections A-D below)	7-13 years*	Multi-center, single-arm, home and hotel clinical study. The study evaluated the safety of the 670G System and its algorithm with the Guardian Sensor in subjects 7 to 13 years.
A Performance Evaluation of the Enlite® and Enlite 3 Glucose Sensor to Support Use in Children; Phase 2 (Enlite 3) (Described in Sections E-H, below)	7-13 years*	Multi-center, prospective, single-sample correlational design without controls. The study demonstrated the measurement performance of the Guardian Sensor 7 days in subjects 2 to 18 years.

*Note: These studies were designed for broader pediatric patient populations (2-13 years for G150247 and 2-18 years for G120262). However, only data for the stipulated patient population, ages 7-13 years, from G150247 was provided in support of this PMA supplement.

Pivotal study: Safety Evaluation of the Hybrid Closed Loop (HCL) System in Pediatric Subjects with Type 1 Diabetes (G150247):

A. Study Design

Subjects were treated between April 18, 2016 and October 09, 2017 and included 105 patients. There were 9 investigational sites.

The pivotal study was a multi-center, single-arm home and hotel clinical evaluation in subjects with type 1 diabetes on insulin pump therapy. The sponsor enrolled 111 subjects (ages 7-13 years) at 9 investigational centers (see subject accountability below).

Of the 111, 106 entered the run-in period. One subject withdrew prior to the start of the study period. Therefore, 105 subjects entered the study period. The 105 study subjects wore the MiniMed 670G pump with the Guardian Link (3) Transmitter, the Guardian Sensor (3) and infusion sets for approximately 3.5 months and participated in all three study phases: a two-week run-in period, a three-month at-home use period, and a 6 days/5 nights hotel study, which occurred during month 1, month 2, or month 3 of the study. Subjects were instructed to use the device in auto mode for the duration of the 3-month at home study.

Run-in period

During the two-week run-in period, subjects used the study pump (670G) with only the sensor augmented pump function activated (all automated features were off).

Prior to wearing study devices, all subjects and their companions were trained on the devices as well as diabetes management principles, such as the treatment of hyperglycemia and hypoglycemia.

At the end of the Run-In period at Run-In Visit 4, subjects 7-13 years of age were asked to undergo a 12 hour (maximum) Frequent Sample Testing procedure to assess the Suspend before Low feature.

At-Home Study Period

Following the two-week run-in period using the Study Pump (670G), a total of 105 subjects participated in a 3-month at-home study period. Prior to entry into Auto Mode, subjects used the pump in Manual Mode during the first 6 days of the study period in order to collect data on insulin utilization and sensor glucose levels. After this 6-day period, the subjects were allowed to enter Auto Mode.

Hotel Study Period

All 105 subjects participated in the Hotel portion of the study (6 days, 5 nights). There was an average of 4-6 subjects participating in each hotel stay. The hotel stays were to occur during the first, second or third month of study, with a minimum of 20 subjects completing the hotel stay each month. The purpose of the hotel portion of the study was to stress the user with sustained daily exercise and unrestricted eating. Subjects participated in daily sustained exercise/activity regimens for a minimum of 4 hours spread throughout the day. With respect to meals, subjects were allowed to eat what they chose.

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 7-13 years at time of screening
   2. Subject age 7 -13 years has 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

   3. Subject must have a minimum daily insulin requirement (Total Daily Dose) of greater than or equal to 8 units.
   4. Subjects 7-13: Subjects and their parent(s)/guardian(s) are willing to participate in an overnight visit at the end of the Run-In period.
   5. Subject 7-13 years of age and their parent(s)/guardian(s) are willing to participate in a Hotel study for the specified duration of Hotel period.
   6. Subject must have companion 18 years or older who will sleep in the same dwelling place every night during the Study period. This requirement may be verified by subject report at screening visit.
   7. Subject is willing to perform $\geq$ 4 finger stick blood glucose measurements daily

8. Subject is willing to perform required sensor calibrations
9. Subject is willing to wear the system continuously throughout the study
10. Subject has a Glycosylated hemoglobin (HbA1c) value less than 10.0% (as processed by Central Lab) at time of screening visit
11. 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.
12. Subject 7 -13 years of age has had pump therapy for greater than 6 months prior to screening (with or without CGM experience)
13. Subjects and their parent(s)/guardian(s) are 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
14. If subject has celiac disease, it has been adequately treated as determined by the investigator
15. Subjects and their parent(s)/guardian(s) are 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)
16. Subjects and their parent(s)/guardian(s)/companions must be able to speak and be literate in English as verified by the investigator

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

Exclusion Criteria:

1. Subject has a history of 2 or more episodes of severe hypoglycemia, which resulted in any the following during the 6 months prior to screening:
   a. Medical assistance (i.e. Paramedics, Emergency Room (ER) or Hospitalization)
   b. Coma
   c. Seizures
2. Subject is unable to tolerate tape adhesive in the area of sensor placement
3. Subject has any unresolved adverse skin condition in the area of sensor placement (e.g., psoriasis, dermatitis herpetiformis, rash, Staphylococcus infection)
4. 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.
5. Subject has a cardiovascular condition which the investigator determines should exclude the subject, i.e. ventricular rhythm disturbance, hypertrophic cardiomyopathy
6. Subject is being treated for hyperthyroidism at time of screening
7. Subject has diagnosis of adrenal insufficiency
8. Subject 7-13 years of age has had DKA in the 6 months prior to screening visit.
9. Subject has taken any oral, injectable, or intravenous (IV) glucocorticoids within 8 weeks from time of screening visit, or plans to take any oral, injectable, or IV glucocorticoids during the course of the study

10. 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
11. Subject 7-13 years of age has been hospitalized or has visited the ER in the 6 months prior to screening resulting in a primary diagnosis of uncontrolled diabetes
12. Subject is currently abusing illicit drugs
13. Subject is currently abusing marijuana.
14. Subject is currently abusing prescription drugs
15. Subject is currently abusing alcohol
16. 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
17. 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
18. Subject has elective surgery planned that requires general anesthesia during the course of the study
19. Subject has a sickle cell disease, hemoglobinopathy; or has received red blood cell transfusion or erythropoietin within 3 months prior to time of screening
20. Subject plans to receive red blood cell transfusion or erythropoietin over the course of study participation
21. Subject diagnosed with current eating disorder such as anorexia or bulimia
22. Subject has been diagnosed with chronic kidney disease that results in chronic anemia
23. Subject has a hematocrit that is below the normal reference range of lab used.
24. Subject is on dialysis
25. Subject has serum creatinine of >2 mg/ dL.

2. Follow-up Schedule

Throughout the study period there were a number of scheduled telephone calls. These calls were meant to make sure that the subject was healthy and to remind them about adherence to study requirements, for example uploading the study pump data to CareLink. During the final study 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 Auto Mode. The analyses used for the various study phases are as follows:

During the Entire Study

Descriptive Endpoints

- The mean change in HbA1c is presented from baseline to end of study
- Change of Total Daily Dose (TDD) of insulin from baseline to end of

study

- Change of weight from baseline to end of study
- Time spent in Auto Mode versus time spent in Manual Mode
- Time in different range (% of sensor glucose): sensor glucose ≤ 50 mg/dL, ≤ 54 mg/dL, ≤60 mg/dL, ≤ 70 mg/dL, 71 mg/dL - ≤180 mg/dL, sensor glucose > 180 mg/dL, > 250 mg/dL, > 350 mg/dL
- Number of Events, area under the curve (AUC) and Time in the high sensor glucose range: sensor glucose (SG) > 180 mg/dL,> 250 mg/dL, >350 mg/dL
- Number of Events, AUC and Time in the low sensor glucose range: sensor glucose ≤ 50 mg/dL, ≤ 54 mg/dL, ≤ 60 mg/dL, and ≤ 70 mg/dL

Safety Data Summarized

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

B. Accountability of Study Cohort

A total of 106 subjects entered the run-in period, 1 subject withdrew during the run-in period and 105 subjects entered the study period. No subject was withdrawn during the study period, therefore 105 subjects completed the study phase.

C. Study Population Demographics and Baseline Parameters

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

Table 5: Study Population Demographics and Baseline Parameters

Characteristic	Number of Subjects =105
Age (Years)	
n	105
Mean (SD)	10.8 (1.8)
Median	11.0
Min, Max	7.0, 13.0
Gender N(%)	
Female	49 (46.7%)
Male	56 (53.3%)
Race N(%)	

Characteristic	Number of Subjects =105
Asian	2 (1.9%)
Black/African American	1 (1.0%)
Other	8 (7.6%)
White	94 (89.5%)
Ethnicity N(%)	
Hispanic/Latino	8 (7.6%)
Non-Hispanic/Non-Latino	97 (92.4%)
Diabetes History(Years)	
n	105
Mean (SD)	5.6 (2.9)
Median	4.9
Min, Max	1.1, 13.0
Height(cm)	
n	104*
Mean (SD)	148.6 (13.8)
Median	148.2
Min, Max	118.3, 184.6
Weight (kg)	
n	104*
Mean (SD)	42.8 (13.0)
Median	40.1
Min, Max	23.4, 83.0
BMI (kg/m^2)	
n	104*
Mean (SD)	19.1 (4.3)
Median	18.0
Min, Max	14.0, 41.0
Baseline HbA1c (%)	
n	105
Mean (SD)	7.9 (0.8)
Median	7.9
Min, Max	5.7, 9.6

* One subject's height and weight were not measured at enrollment

D. Safety and Effectiveness Results

1. Safety Results

The safety of the 670G System was assessed by evaluation of the incidence of all adverse device events (ADEs), serious adverse device events (SADEs), and unanticipated adverse device events (UADEs) experienced by study subjects. AEs were listed in terms of severity and relationship to the device.

There was one report of a serious adverse event. This event was an episode of DKA that occurred prior to the subject beginning use of the 670G system, and therefore the event was not related to the 670G system or the other components of the 670G system.

There were no reports of unanticipated serious adverse device effects.

There were no reports of severe hypoglycemia events.

There was one report of a non-SADE. This event involved anxiety associated with sensor insertion that progressed throughout the subject's participation in the study.

There were 5 procedure-related events:

- neurocardiogenic syncope
- headache
- angioedema
- hyperglycemia
- skin irritation

There were 104 severe hyperglycemia events reported:

Severe hyperglycemia was defined in the protocol as a blood glucose concentration >300 mg/dL with blood ketones >0.6mmol/L or accompanied by symptoms of nausea, vomiting or abdominal pain.

Of the 104 reported severe hyperglycemia events, 62 were thought to be device-related. The majority of the device-related severe hyperglycemia events were believed to be due to infusion set issues (occlusion, bent cannula or cannula pull out). Other infrequently (2 events or less) reported causes of the device related severe hyperglycemia events include events associated with both automated and manual functionalities of the 670G System (safe basal, suspend before low suspension, automatic and manual suspensions). (See Table 6 below).

Table 6. Study Period Severe Hyperglycemia

Cause	Total
Infusion set change	**28**
Occlusion alarm	**12**
Infusion set fell out	**7**
Bent /Kinked Cannula	**5**
Infusion set change/safe basal	**3**
Safe basal	**2**
Suspend before low suspension	**1**
Automatic & manual suspensions	**1**
Unclipped infusion set	**1**
Internal Battery Connector Resistance	**1**
Manual suspension and safe basal	**1**
Total	**62**

Of these 62 reported device related severe hyperglycemia events, all events were reported to have resolved without sequalae. There were no reports of emergency room visits or hospitalizations relating to these 62 reported device related severe hyperglycemia events.

Of the 42 non-device related severe hyperglycemia events reported, all events were reported to have recovered without sequelae. The majority of reported causes of these non-device related severe hyperglycemia events were reported to be due to illness, stress, and incorrect meal boluses. Of these 42 non-device related severe hyperglycemia events, one event resulted in a visit to the emergency room with the subject being discharged home on the same day. This event was reported to have resolved without sequelae.

2. Effectiveness Results

System Performance: Pivotal Study (G150247)

As stated above, the study performed was an observational study and only designed to evaluate system safety. The data below describe how the device performed during the pivotal study. The study was not designed to determine the effectiveness of the device compared to alternative treatments such as manual daily injections or non-automated insulin pump therapy.

The table below provides an overall summary of the run-in phase and study phase (home and hotel) for all subjects in the study. The data presented in this table includes information about subjects' glucose levels, insulin delivered and weight during run-in versus study phases.

Table 7: Percent of Time within Glucose Ranges, Mean Insulin Delivery, and Mean Weight

of Subjects during Run-in and Study Phases

Parameter	Run-In	Study
Sensor glucose, *mean* ± *SD* (median) mg/dL	168.6±21.6(168.0, 154.5-183.6)	161.7±12.4(161.9, 153.5-169.0)
Sensor Glucose Range (mg/dL)	Percent of Time with Sensor Glucose Level in Range Mean ± SD (95% CI), %	
≤ 50 mg/dL	0.85±1.17(0.62, 1.07)	0.55±0.51(0.45, 0.64)
≤ 54 mg/dL	1.29±1.55(0.99, 1.59)	0.81±0.68(0.68, 0.95)
≤ 60 mg/dL	2.24±2.27(1.80, 2.68)	1.41±0.98(1.22, 1.60)
≤ 70 mg/dL	4.74±3.85(4.00, 5.49)	2.99±1.64(2.68, 3.31)
71 −≤ 180 mg/dL	56.16±11.35(53.96, 58.35)	65.01±7.67(63.53, 66.50)
> 180 mg/dL	39.10±12.80(36.63, 41.58)	31.99±7.67(30.51, 33.48)
> 250 mg/dL	13.26±7.74(11.76, 14.76)	10.31±5.15(9.31, 11.30)
> 300 mg/dL	4.73±3.80(3.99, 5.46)	3.73±2.74(3.20, 4.26)
> 350 mg/dL	1.60±1.73(1.26, 1.93)	1.21±1.19(0.98, 1.44)
Within-day SD of sensor glucose –*mean* ± *SD* (*median, interquartile range*) mg/dL	57.7±8.3(58.4, 52.2-65.0)	54.7±7.5(55.0, 49.7-59.1)
Within-day coefficient of variation of sensor glucose (%)–*mean* ± *SD* (*median, interquartile range*) mg/dL	34.8±4.3(34.4, 32.0-37.8)	33.7±3.1(33.7, 31.4-35.8)
Glycated hemoglobin –*mean* ± *SD (median, interquartile range), %*	7.9±0.8(7.9, 7.2-8.4)	7.5±0.6(7.5, 7.1-7.8)
Total daily dose of insulin –*mean* ± *SD (median, interquartile range), U*	35.7±14.6(32.1, 24.4-45.0)	38.5±15.5(34.3, 27.0-50.1)
Weight –*mean* ± *SD (median, interquartile range), kg*	42.8±13.0(40.1, 32.4-51.6)	44.9±13.4(42.3, 33.8-53.3)

The baseline HbA1c value was collected at the first office visit for subjects during the study phase. The end of study HbA1c was collected at the last visit of the study phase. A summary of HbA1c data is provided in the table below.

Table 8: Percent Change in HbA1c from Baseline to End of Study

	Baseline % (SD)	**End of Study % (SD)**
Number of Subjects	105	105
HbA1c, %, Mean(SD)	7.9 (0.8)	7.5 (0.6)
HbA1c %, Median	7.9	7.5
95% Confidence Interval	(7.7, 8.0)	(7.4, 7.6)
HbA1c, %, Min, Max	5.7, 9.6	6.4, 9.3

The table below provides data regarding the subject baseline HbA1c collected at the beginning of the study and the number of subjects who with decreased, unchanged, or increased HbA1c values at the end of the study.

Table 9: Number of subjects with change in HbA1C at different baselines

HbA1c Range	**Number of Subject (%) with Change in HbA1c**				
Baseline HbA1c (%)	**Decrease > 1%**	**Decrease > 0 to 1%**	**No Change**	**Increase > 0 to 1%**	**Increase > 1%**
5%≤ **HbA1c** <6%	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)
6%≤ **HbA1c** <7%	0 (0.0%)	1 (1.0%)	0 (0.0%)	9 (8.6%)	0 (0.0%)
7%≤ **HbA1c** <8%	3 (2.9%)	22 (21.0%)	6 (5.7%)	16 (15.2%)	0 (0.0%)
8%≤ **HbA1c** <9%	9 (8.6%)	21 (20.0%)	3 (2.9%)	4 (3.8%)	0 (0.0%)
9%≤ **HbA1c**<10%	4 (3.8%)	6 (5.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Overall	16 (15.2%)	50 (47.6%)	9 (8.6%)	30 (28.6%)	0 (0.0%)

The table below summarizes time spent in Auto Mode and summary of sensor wear, from start of Auto-Mode (Day 7 of the Study Phase) until the end of the study period.

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

Category	**Percentage of Time**
Time spent wearing sensor	95.1%
Time spent not wearing sensor	4.9%
Auto Mode (core algorithm)	71.9%
Auto Mode (safe basal)	6.6%
Time spent in Manual Mode	21.5%

Guardian Sensor Performance Study (G120262)- A Performance Evaluation of the Enlite® and Enlite 3 Glucose Sensor to Support Use in Children; Phase 2 (Enlite 3):

E. Study Design

This study was performed to assess the analytical performance of the Guardian sensor. It ran between May12, 2015 and December 13, 2016 and included 61 subjects (different from subjects who participated in the pivotal study above). There were 11 investigational sites.

This study was a prospective, single arm, multi-center, in-clinic study. All subjects wore one receiver, one transmitter, one transmitter used as a recorder, and two sensors.

Subjects wore the Guardian Sensor (3) in the abdomen and buttock insertion sites for a 7-day training period (that included a minimum 6 days of sensor wear), followed by a 7-day study period. During the study period, each subject participated in one in-clinic, frequent sample testing (FST) evaluation. FST occurred at the beginning (Day 1), middle (Day 3) or end (Day 7) of the Guardian sensor system use. During these FST sessions, intravenous (IV) blood samples were drawn every 5 to 15 minutes and analyzed for plasma blood glucose levels using the comparator method (CM). The CM is this study was the Yellow Springs Instrument 2300 Stat Plus Glucose Lactate Analyzer. FST with the CM lasted approximately 6 hours during the in-clinic visit.

Subjects were randomly assigned to one of three sensor insertion combinations; abdomen/abdomen (17 subjects), buttock/buttock (10 subjects), or abdomen/buttock (23 subjects). Subjects were randomized to one of 10 groups that determined when they participated in the in-clinic frequent sample testing.

Subjects continued with their current diabetes regimen independent of the study devices. Subjects were instructed by the investigational center that they were not to use the investigational devices for the management of their diabetes.

There was no control group as this study was an observational study to observe the accuracy and precision of the Guardian sensor. Accuracy was assessed by comparing the sensor values to the CM, and precision of the sensor system was assessed by comparing sensor values to each other in subjects wearing two sensors.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the Guardian sensor study was limited to subjects who met the following inclusion criteria:

   1. Subject is 7-13 years of age at time of screening (which was a subset of the entire study population)
   2. Subject has been diagnosed with insulin requiring diabetes mellitus for at least one year.
   3. Subject is willing to perform greater than or equal to 4 finger stick blood glucose measurements daily

4. Subject is willing to perform required sensor calibrations
5. Subject is willing to wear the system (Guardian Mobile application, pumps, sensors, meter) continuously throughout the study
6. Adequate venous access for subjects requiring IV for their FST, as assessed by investigator or appropriate staff

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

1. Subject is unable to tolerate tape adhesive in the area of sensor placement
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. Females of child-bearing potential who have a positive pregnancy test at screening or plans to become pregnant during the course of the study
5. Subjects with hematocrit lower than the normal age specific reference range per central or local lab testing

2. Follow-up Schedule

At the end of the study, subjects removed all study devices. Upon removal, all the Sensor insertion sites were examined and evaluated by the study staff. Sensors were visually inspected at the site. Study investigators documented any Adverse Device Effects (including skin irritations) and evaluated safety issues related to system use during the study. No long-term follow up was included in this study protocol.

3. Clinical Endpoints

Because this was an observational study, it did not include traditional analysis of clinical endpoints. The data were presented using multiple analyses as described in the Study Results section below.

Safety of the sensor was determined by skin and insertion site reactions.

F. Accountability of Study Cohort

Of the 61 subjects that entered the study, 3 completed Phase 1 (Enlite phase) of the study without participating in Phase 2 (Enlite 3 Phase). An additional eight (8) subjects withdrew before entering Phase 2 (Enlite 3 phase) for the following reasons:

- One subject decided not to be in the study any longer.
- Two subjects withdrew due to school schedule
- One subject withdrew due to work and school schedule
- One subject withdrew because subject did not feel comfortable inserting sensors at home.
- One subject withdrew because subject did not like first sensor insertion (after training)
- One subject withdrew because of major psychosocial issues and stress in family

- One subject withdrew because subject found wearing sensor too difficult – too much stimulus and information for patient to track

Among the 50 randomized subjects, 5 subjects did not complete the study for the following reasons:

- Four subjects withdrew due to repeated sensor failures
- One subject withdrew due to school schedule

A total of 44 subjects underwent frequent sample testing and completed the study. Twenty-one (21) subjects completed the first frequent sample testing on day 1, 13 subjects completed frequent sample testing on day 3, and 10 subjects completed frequent sample testing on day 7. One (1) subject completed the study, but did not complete frequent sample testing.

G. Study Population Demographics and Baseline Parameters

Table 11: Study Population Demographics and Baseline Parameters

Characteristic	All Subjects N=50
Age (Years)	
Number of Subjects	50
Mean (SD)	11.4 (1.53)
Median	12
Min, Max	8.0 , 13.0
Gender, Number(%)	
Female not of child bearing potential	17 (34.0%)
Female of child bearing potential	6 (12.0%)
Male	27 (54.0%)
Race, Number(%)	
Asian	1 (2.0%)
Other	6 (12.0%)
White	43 (86.0%)
Ethnicity, Number(%)	
Hispanic/Latino	6 (12.0%)
Non-Hispanic/Non-Latino	43 (86.0%)
Subject refused	1 (2.0%)
Height (cm)	
Number of Subjects	50
Mean (SD)	153.5 (13.24)
Median	154
Min, Max	125.0 , 180.3
Weight (kg)	
Number of Subjects	50
Mean (SD)	49.8 (16.86)

Characteristic	All Subjects N=50
Median	47
Min, Max	23.0 , 104.5
Body Mass Index (kg/m2)	
Number of Subjects	50
Mean (SD)	20.7 (5.08)
Median	19.3
Min, Max	14.7 , 36.9
A1C (%)	
Number of Subjects	50
Mean (SD)	8.0 (0.99)
Median	8
Min, Max	6.0 , 11.0
Hematocrit (%)	
Number of Subjects	50
Mean (SD)	41.9 (2.49)
Median	41.9
Min, Max	37.2 , 49.9

H. Safety and Effectiveness Results

1. Safety Results

The safety of the Guardian Sensor (3) was assessed by evaluation of the incidence of all adverse events, ADEs, SADEs, and UADEs experienced by study subjects. AEs were listed in terms of severity and relationship to device. Sensor insertion site and adhesive area were examined for erythema, edema and infection. The local skin reactions from the insertion site or the adhesive were also evaluated.

There were 10 adverse events reported during the study as summarized below. None of these events were believed to be device-related All adverse events were resolved and subjects recovered completely without residual sequelae:

- There was one report of influenza virus B.
- There were two reports of gastroenteritis.
- There were two reports of upper respiratory infection.
- There was one report of a sore throat.
- There was one report of a vasovagal event.
- There was one report of abrasions due to falling off a scooter.
- There was one report of severe hyperglycemia secondary to influenza B
- There was one report of otitis media.

There were no reports of subject death.
There were no reports of device-related SAEs. There were no reports of non-

device-related SAEs.
There were no reports of DKA.
There were no reports of severe hyperglycemia.
There were no reports of severe hypoglycemia.
There were no reports of device-related adverse events.
The incidence of adverse events directly related to the CGM in the intended use population is not expected to differ significantly from the event rate observed during the Sensor accuracy study or those observed for other approved CGM devices. Based on (FDA-analyzed) post-market adverse event reports for similar CGM devices, no additional concerns regarding adverse events were raised for CGMs.

2. Effectiveness Results

Study results from the Guardian sensor study are presented in Tables 12 to 46. Results are presented below by abdominal insertion site followed by buttock insertion site.

The sensor must be calibrated at least twice per day (every 12 hours). However, the sponsor recommends users calibrate more often for best results (3 to 4 times per day). Most tables below represent data for minimal calibration (every 12 hours). Please see table headers to understand calibration frequency for each analysis.

Abdomen Insertion Site

Tables 12 and 13 below provide the Guardian Sensor (3) values and the percent of data points that fell within 15, 20, 30, 40, and >40 mg/dL, or percent, of a specific CM glucose range when the sensor worn in the abdomen was calibrated every 12 hours after: Days 1, 3, and 7 (table 12); Day 1 only (table 13), respectively.

Table 12. Agreement (%) of Sensor-CM Paired Points (15/15%- greater than 40/40%) Stratified by Different CM Glucose Ranges, Calibrated every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age, ***Days 1, 3, and 7 combined***

CM Glucose Ranges (mg/dL)	Number of Subjects	Number of CGM-CM Pairs	Percent of CGM Within 15/15% of CM	Percent of CGM Within 20/20% of CM	Percent of CGM Within 30/30% of CM	Percent of CGM Within 40/40% of CM	Percent of CGM Within >40/40% of CM
Overall	30	733	78.9	87.7	95.9	98.9	1.1
≥40-60*	2	4	50	50	75	100	0
>60-80*	5	20	70	80	90	95	5
>80-180	27	378	74.1	83.1	92.9	98.1	1.9
>180-300	26	290	83.1	93.1	100	100	0
>300-350	6	32	100	100	100	100	0
>350-400	3	9	100	100	100	100	0

**For glucose ranges ≤ 80 mg/dL, agreement was based on 15/20/30/40 mg/dL. Note: Sensor glucose readings are within 40-400 mg/dL*

Table 13. Agreement (%) of Sensor-CM Paired Points (15/15%- greater than 40/40%) Stratified by Different CM Glucose Ranges, Calibrated every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age, ***Day 1***

CM Glucose Ranges (mg/dL)	Number of Subjects	Number of CGM-CM Pairs	Percent of CGM Within 15/15% of CM	Percent of CGM Within 20/20% of CM	Percent of CGM Within 30/30% of CM	Percent of CGM Within 40/40% of CM	Percent of CGM Within >40/40% of CM
Overall	16	403	81.9	90.6	96.5	99	1
≥40-60*	1	2	100	100	100	100	0
>60-80*	3	11	63.6	72.7	90.9	100	0
>80-180	14	196	75.5	84.2	93.4	98	2
>180-300	15	160	86.9	97.5	100	100	0
>300-350	3	27	100	100	100	100	0
>350-400	2	7	100	100	100	100	0

**For glucose ranges ≤ 80 mg/dL, agreement was based on 15/20/30/40 mg/dL. Note: Sensor glucose readings are within 40-400 mg/dL*

The following tables (14 to 17) show the percentage of concurring CGM readings compared to CM values for sensors worn in the abdomen. With ideal performance, the CGM readings would match the CM values. For example, with perfect concurrence, the shaded boxes in the tables below would be 100 percent.

Tables 14 and 15 show the concurrence of the CGM values compared to CM values when calibrating every 12 hours, after Days 1, 3, and 7.

Tables 16 and 17 show the concurrence of the CGM values compared to CM values when calibrating three to four times per day, after Days 1, 3, and 7.

Table 14. Concurrence of CM values and CGM readings using CM glucose ranges; Calibrating every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age, Overall

CM Glucose Ranges (mg/dL)	Percent of Matched Pairs-in Each CGM Glucose Range for Each CM Glucose Range											
	CGM (mg/dL)											
	# of Paired CGM-CM	<40	≥40-60	>60-80	>80-120	>120-160	>160-200	>200-250	>250-300	>300-350	>350-400	>400
>=40-60	6	33.3% (2/6)	33.3% (2/6)	0.0% (0/0)	33.3% (2/6)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>60-80	20	0.0% (0/0)	10.0% (2/20)	55.0% (11/20)	35.0% (7/20)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>80-120	124	0.0% (0/0)	4.8% (6/124)	13.7% (17/124)	66.1% (82/124)	15.3% (19/124)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>120-160	169	0.0% (0/0)	0.0% (0/0)	0.6% (1/169)	21.3% (36/169)	62.1% (105/169)	15.4% (26/169)	0.6% (1/169)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>160-200	160	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	1.9% (3/160)	25.0% (40/160)	64.4% (103/160)	8.8% (14/160)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>200-250	151	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	1.3% (2/151)	40.4% (61/151)	56.3% (85/151)	2.0% (3/151)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>250-300	64	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	32.8% (21/64)	64.1% (41/64)	3.1% (2/64)	0.0% (0/0)	0.0% (0/0)
>300-350	32	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	40.6% (13/32)	59.4% (19/32)	0.0% (0/0)	0.0% (0/0)
>350-400	9	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	88.9% (8/9)	11.1% (1/9)	0.0% (0/0)

Table 15. Concurrence of CM values and CGM readings using CM glucose ranges; Calibrating three to four times per day, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age, Day Overall

	Percent of Matched Pairs-in Each CGM Glucose Range for Each CM Glucose Range											
	CGM (mg/dL)											
CM Glucose Ranges (mg/dL)	**Number of Paired CGM-CM**	**<40**	**≥40-60**	**>60-80**	**>80-120**	**>120-160**	**>160-200**	**>200-250**	**>250-300**	**>300-350**	**>350-400**	**>400**
≥40-60	2	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	100.0% (2/2)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>60-80	18	0.0% (0/0)	0.0% (0/0)	61.1% (11/18)	38.9% (7/18)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>80-120	120	0.0% (0/0)	3.3% (4/120)	15.8% (19/120)	67.5% (81/120)	13.3% (16/120)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>120-160	162	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	17.9% (29/162)	64.8% (105/162)	16.7% (27/162)	0.6% (1/162)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>160-200	161	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	1.2% (2/161)	25.5% (41/161)	65.2% (105/161)	8.1% (13/161)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>200-250	145	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	1.4% (2/145)	42.8% (62/145)	53.8% (78/145)	2.1% (3/145)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>250-300	61	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	32.8% (20/61)	65.6% (40/61)	1.6% (1/61)	0.0% (0/0)	0.0% (0/0)
>300-350	32	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	37.5% (12/32)	62.5% (20/32)	0.0% (0/0)	0.0% (0/0)
>350-400	9	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	55.6% (5/9)	44.4% (4/9)	0.0% (0/0)

Table 16. Concurrence of CGM readings and CM values using CGM glucose ranges; Calibrating every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age, Day Overall

	Percent of Matched Pairs-in Each CM Glucose Range for Each CGM Glucose Range											
	CM (mg/dL)											
CGM Glucose Ranges (mg/dL)	**Number of Paired CGM-CM Values**	**<40**	**≥40-60**	**>60-80**	**>80-120**	**>120-160**	**>160-200**	**>200-250**	**>250-300**	**>300-350**	**>350-400**	**>400**
<40	2	0.0% (0/0)	100.0% (2/2)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
≥40-60	10	0.0% (0/0)	20.0% (2/10)	20.0% (2/10)	60.0% (6/10)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>60-80	29	0.0% (0/0)	0.0% (0/0)	37.9% (11/29)	58.6% (17/29)	3.4% (1/29)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>80-120	130	0.0% (0/0)	1.5% (2/130)	5.4% (7/130)	63.1% (82/130)	27.7% (36/130)	2.3% (3/130)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>120-160	166	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	11.4% (19/166)	63.3% (105/166)	24.1% (40/166)	1.2% (2/166)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>160-200	190	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	13.7% (26/190)	54.2% (103/190)	32.1% (61/190)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>200-250	121	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.8% (1/121)	11.6% (14/121)	70.2% (85/121)	17.4% (21/121)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>250-300	57	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	5.3% (3/57)	71.9% (41/57)	22.8% (13/57)	0.0% (0/0)	0.0% (0/0)
>300-350	29	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	6.9% (2/29)	65.5% (19/29)	27.6% (8/29)	0.0% (0/0)
>350-400	1	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	100.0% (1/1)	0.0% (0/0)

Table 17. Concurrence of CGM readings and CM values using CGM glucose ranges; Calibrating three to four times per day, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age, Day Overall

	Percent of Matched Pairs-in Each CM Glucose Range for Each CGM Glucose Range											
	CM (mg/dL)											
CGM Glucose Ranges (mg/dL)	**Number of Paired CGM-CM Values**	**<40**	**≥40-60**	**>60-80**	**>80-120**	**>120-160**	**>160-200**	**>200-250**	**>250-300**	**>300-350**	**>350-400**	**>400**
≥40-60	4	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	100.0% (4/4)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>60-80	30	0.0% (0/0)	0.0% (0/0)	36.7% (11/30)	63.3% (19/30)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>80-120	121	0.0% (0/0)	1.7% (2/121)	5.8% (7/121)	66.9% (81/121)	24.0% (29/121)	1.7% (2/121)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>120-160	164	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	9.8% (16/164)	64.0% (105/164)	25.0% (41/164)	1.2% (2/164)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>160-200	194	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	13.9% (27/194)	54.1% (105/194)	32.0% (62/194)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>200-250	112	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.9% (1/112)	11.6% (13/112)	69.6% (78/112)	17.9% (20/112)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>250-300	55	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	5.5% (3/55)	72.7% (40/55)	21.8% (12/55)	0.0% (0/0)	0.0% (0/0)
>300-350	26	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	3.8% (1/26)	76.9% (20/26)	19.2% (5/26)	0.0% (0/0)
>350-400	4	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	100.0% (4/4)	0.0% (0/0)

Table 18 below provides data representing sensor accuracy in the abdomen over specific glucose rates of change. The concurrence tables below provide the percent of matched CM pairs to CGM values over specific glucose rates of change for sensors worn in the abdomen calibrated every 12 hours.

Table 18. Calibration every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age

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	19	47.4% (9/19)	47.4% (9/19)	0.0% (0/19)	5.3% (1/19)	0.0% (0/19)	0.0% (0/19)
[-2, -1)	107	2.8% (3/107)	31.8% (34/107)	60.7% (65/107)	3.7% (4/107)	0.9% (1/107)	0.0% (0/107)
[-1, 0)	276	0.7% (2/276)	5.8% (16/276)	71.7% (198/276)	21.0% (58/276)	0.7% (2/276)	0.0% (0/276)
[0, 1]	209	0.0% (0/209)	1.0% (2/209)	22.5% (47/209)	62.2% (130/209)	13.9% (29/209)	0.5% (1/209)
(1, 2]	98	0.0% (0/98)	0.0% (0/98)	1.0% (1/98)	37.8% (37/98)	59.2% (58/98)	2.0% (2/98)
>2	23	0.0% (0/23)	0.0% (0/23)	4.3% (1/23)	8.7% (2/23)	30.4% (7/23)	56.5% (13/23)

Tables 19 and 20 below provide the Guardian sensor values and the percent difference with respect to CGM values when the sensor worn in the abdomen was calibrated every 12 hours, or three to four times per day, respectively.

Table 19. CGM Difference to CM within CGM Glucose Ranges, Calibrating Every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age

CGM Glucose Ranges (mg/dL)	Number of Paired CGM-CM Pairs	Mean Absolute Percent Difference (%)	Median Absolute Percent Difference (%)
Overall	733	11.73	9.16
40-60*	10	25.05	28.28
61-80*	29	20.59	17.7
81-180	415	12.18	10.27
181-300	249	7.93	6.9
301-350	29	7.07	6.74
351-400	1	5.2	5.2

**For glucose ranges ≤ 80 mg/dL, the differences in mg/dL are included instead of percent difference (%). Note: Sensor glucose readings are within 40-400 mg/dL.*

Table 20. CGM Difference to CM within CGM Glucose Ranges, Calibrating three to four times per day, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age

CGM Glucose Ranges (mg/dL)	Number of Paired CGM-CM Pairs	Mean Absolute Percent Difference (%)	Median Absolute Percent Difference (%)
Overall	710	10.78	8.56
40-60*	4	30.05	32.68
61-80*	30	17.82	18.23
81-180	395	11.53	10.14
181-300	251	7.91	7.07
301-350	26	5.13	4.19
351-400	4	3.85	4.01

**For glucose ranges ≤ 80 mg/dL, the differences in mg/dL are included instead of percent difference (%). Note: Sensor glucose readings are within 40-400 mg/dL.*

Table 21 shows sensor stability (accuracy over time) in the abdomen by comparing the CM values collected during frequent sample testing days 1, 3, and 7 to their paired sensor points. The table stratifies the paired CM-sensor data by 15/15, 20/20, 30/30, 40/40 and >40/40 mg/dL and percent, respectively.

Table 21. Sensor Stability (accuracy over time) for Calibration every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age

Day of Wear	Number of Paired System CM	Mean absolute percent difference (%)	Median absolute percent difference (%)	Percent within 15/15% CM	Percent within 20/20% CM	Percent within 30/30% CM	Percent within 40/40% CM	Percent greater than 40/40% CM
1	403	9.8	8.7	81.9	90.6	96.5	99.0	1.0
3	236	9.6	8.9	79.2	88.6	100.0	100.0	0.0
7	94	15.3	9.6	64.9	73.4	83.0	95.7	4.3

Tables 22 and 23 below provide the number and percentage of CM measurements collected while the continuous glucose monitor read 'low' (< 40 mg/dL), or 'high' (> 400 mg/dL) for sensors worn in the abdomen calibrated every 12 hours.

Table 22. The Number and Percentage of CM values collected when CGM readings displayed 'Low' (less than 40 mg/dL); calibrating every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age

CGM Readings	CGM-CM pairs	<55	<60	<70	<80	>80	Total
'LOW'	Cumulative, n	2	2	2	2	0	2
	Cumulative %	100%	100%	100%	100%	0%	

Table 23. The Number and Percentage of CM values collected when CGM readings displayed 'High' (more than 400 mg/dL); calibrating every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age

CGM Readings	CGM-CM pairs	>340	>320	>280	>240	<240	Total
'HIGH'	Cumulative, n	0	0	0	0	0	0
	Cumulative %	0%	0%	0%	0%	0%	

Pump Alert Performance using the Abdomen Sensor Insertion Site

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

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. 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 24. Glucose TRUE Alert Performance, Calibrating every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			**Predictive Only**			**Threshold & Predictive**		
	mg/dL	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**
Glucose True Alert Rate: Low glucose Alerts	**50**	33.3% (1/3, 3)	33.3% (1/3, 3)	**50**	12.5% (1/8, 7)	12.5% (1/8, 7)	**50**	18.2% (2/11, 7)	18.2% (2/11, 7)
	55	25.0% (1/4, 4)	25.0% (1/4, 4)	**55**	9.1% (1/11, 7)	9.1% (1/11, 7)	**55**	13.3% (2/15, 7)	13.3% (2/15, 7)
	60	25.0% (1/4, 4)	25.0% (1/4, 4)	**60**	8.3% (1/12, 8)	8.3% (1/12, 8)	**60**	12.5% (2/16, 8)	12.5% (2/16, 8)
	70	44.4% (4/9, 8)	44.4% (4/9, 8)	**70**	28.6% (4/14, 9)	14.3% (2/14, 9)	**70**	36.4% (8/22, 9)	27.3% (6/22, 9)
	80	33.3% (4/12, 9)	33.3% (4/12, 9)	**80**	31.6% (6/19, 14)	15.8% (3/19, 14)	**80**	32.3% (10/31, 14)	22.6% (7/31, 14)
	90	55.0% (11/20, 16)	55.0% (11/20, 16)	**90**	46.2% (12/26, 16)	30.8% (8/26, 16)	**90**	47.7% (21/44, 17)	38.6% (17/44, 17)

	Threshold Only			Predictive Only			Threshold & Predictive		
	mg/dL	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**
Glucose True Alert Rate: High glucose Alerts	**300**	77.8% (7/9, 6)	77.8% (7/9, 6)	**300**	44.4% (8/18, 13)	44.4% (8/18, 13)	**300**	55.6% (15/27, 13)	55.6% (15/27, 13)
	250	81.3% (13/16, 14)	81.3% (13/16, 14)	**250**	53.1% (17/32, 23)	46.9% (15/32, 23)	**250**	63.0% (29/46, 23)	58.7% (27/46, 23)
	220	87.5% (21/24, 19)	87.5% (21/24, 19)	**220**	60.0% (27/45, 28)	57.8% (26/45, 28)	**220**	68.2% (45/66, 28)	66.7% (44/66, 28)
	180	78.4% (40/51, 29)	78.4% (40/51, 29)	**180**	66.2% (47/71, 30)	66.2% (47/71, 30)	**180**	70.5% (79/112, 30)	70.5% (79/112, 30)

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

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); or
- 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); or
- 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 25. Glucose FALSE Alert Performance, Calibrating every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			**Predictive Only**			**Threshold & Predictive**		
	mg/dL	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**
Glucose False Alert Rate: Low Glucose Alerts	**50**	66.7% (2/3, 3)	66.7% (2/3, 3)	**50**	87.5% (7/8, 7)	87.5% (7/8, 7)	**50**	81.8% (9/11, 7)	81.8% (9/11, 7)
	55	75.0% (3/4, 4)	75.0% (3/4, 4)	**55**	90.9% (10/11, 7)	90.9% (10/11, 7)	**55**	86.7% (13/15, 7)	86.7% (13/15, 7)
	60	75.0% (3/4, 4)	75.0% (3/4, 4)	**60**	91.7% (11/12, 8)	91.7% (11/12, 8)	**60**	87.5% (14/16, 8)	87.5% (14/16, 8)

	Threshold Only			Predictive Only			Threshold & Predictive		
	mg/dL	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**
Glucose False Alert Rate: Low Glucose Alerts	**70**	55.6% (5/9, 8)	55.6% (5/9, 8)	**70**	71.4% (10/14, 9)	85.7% (12/14, 9)	**70**	63.6% (14/22, 9)	72.7% (16/22, 9)
	80	66.7% (8/12, 9)	66.7% (8/12, 9)	**80**	68.4% (13/19, 14)	84.2% (16/19, 14)	**80**	67.7% (21/31, 14)	77.4% (24/31, 14)
	90	45.0% (9/20, 16)	45.0% (9/20, 16)	**90**	53.8% (14/26, 16)	69.2% (18/26, 16)	**90**	52.3% (23/44, 17)	61.4% (27/44, 17)
Glucose False Alert Rate: High Glucose Alerts	**300**	22.2% (2/9, 6)	22.2% (2/9, 6)	**300**	55.6% (10/18, 13)	55.6% (10/18, 13)	**300**	44.4% (12/27, 13)	44.4% (12/27, 13)
	250	18.8% (3/16, 14)	18.8% (3/16, 14)	**250**	46.9% (15/32, 23)	53.1% (17/32, 23)	**250**	37.0% (17/46, 23)	41.3% (19/46, 23)
	220	12.5% (3/24, 19)	12.5% (3/24, 19)	**220**	40.0% (18/45, 28)	42.2% (19/45, 28)	**220**	31.8% (21/66, 28)	33.3% (22/66, 28)
	180	21.6% (11/51, 29)	21.6% (11/51, 29)	**180**	33.8% (24/71, 30)	33.8% (24/71, 30)	**180**	29.5% (33/112, 30)	29.5% (33/112, 30)

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

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 26. Glucose Correct Detection Alert Performance, Calibrating every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			Predictive Only			Threshold & Predictive		
	mg/dL	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**
Glucose Correct Detection Rate: Low Glucose Alerts	**50**	100.0% (1/1, 1)	100.0% (1/1, 1)	**50**	100.0% (1/1, 1)	100.0% (1/1, 1)	**50**	100.0% (1/1, 1)	100.0% (1/1, 1)
	55	50.0% (1/2, 2)	50.0% (1/2, 2)	**55**	50.0% (1/2, 2)	50.0% (1/2, 2)	**55**	50.0% (1/2, 2)	50.0% (1/2, 2)
	60	50.0% (1/2, 2)	50.0% (1/2, 2)	**60**	50.0% (1/2, 2)	50.0% (1/2, 2)	**60**	50.0% (1/2, 2)	50.0% (1/2, 2)
	70	80.0% (4/5, 5)	80.0% (4/5, 5)	**70**	80.0% (4/5, 5)	40.0% (2/5, 5)	**70**	80.0% (4/5, 5)	80.0% (4/5, 5)
	80	66.7% (4/6, 5)	66.7% (4/6, 5)	**80**	83.3% (5/6, 5)	50.0% (3/6, 5)	**80**	83.3% (5/6, 5)	66.7% (4/6, 5)
	90	91.7% (11/12, 10)	91.7% (11/12, 10)	**90**	91.7% (11/12, 10)	66.7% (8/12, 10)	**90**	91.7% (11/12, 10)	91.7% (11/12, 10)
Glucose Correct Detection Rate: High Glucose Alerts	**300**	80.0% (8/10, 6)	80.0% (8/10, 6)	**300**	100.0% (10/10, 6)	90.0% (9/10, 6)	**300**	100.0% (10/10, 6)	90.0% (9/10, 6)
	250	77.8% (14/18, 14)	77.8% (14/18, 14)	**250**	88.9% (16/18, 14)	83.3% (15/18, 14)	**250**	88.9% (16/18, 14)	83.3% (15/18, 14)
	220	92.6% (25/27, 21)	85.2% (23/27, 21)	**220**	96.3% (26/27, 21)	88.9% (24/27, 21)	**220**	96.3% (26/27, 21)	88.9% (24/27, 21)
	180	95.1% (39/41, 26)	95.1% (39/41, 26)	**180**	100.0% (41/41, 26)	100.0% (41/41, 26)	**180**	100.0% (41/41, 26)	100.0% (41/41, 26)

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

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 27. Glucose Missed Detection Alert Performance, Calibrating every 12 hours, Abdominal Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			**Predictive Only**			**Threshold & Predictive**		
	mg/dL	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**
Glucose Missed Detection Rate: Low Glucose Alerts	**50**	0.0% (0/1, 1)	0.0% (0/1, 1)	**50**	0.0% (0/1, 1)	0.0% (0/1, 1)	**50**	0.0% (0/1, 1)	0.0% (0/1, 1)
	55	50.0% (1/2, 2)	50.0% (1/2, 2)	**55**	50.0% (1/2, 2)	50.0% (1/2, 2)	**55**	50.0% (1/2, 2)	50.0% (1/2, 2)
	60	50.0% (1/2, 2)	50.0% (1/2, 2)	**60**	50.0% (1/2, 2)	50.0% (1/2, 2)	**60**	50.0% (1/2, 2)	50.0% (1/2, 2)
	70	20.0% (1/5, 5)	20.0% (1/5, 5)	**70**	20.0% (1/5, 5)	60.0% (3/5, 5)	**70**	20.0% (1/5, 5)	20.0% (1/5, 5)
	80	33.3% (2/6, 5)	33.3% (2/6, 5)	**80**	16.7% (1/6, 5)	50.0% (3/6, 5)	**80**	16.7% (1/6, 5)	33.3% (2/6, 5)
	90	8.3% (1/12, 10)	8.3% (1/12, 10)	**90**	8.3% (1/12, 10)	33.3% (4/12, 10)	**90**	8.3% (1/12, 10)	8.3% (1/12, 10)

	Threshold Only			Predictive Only			Threshold & Predictive		
	mg/dL	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**
Glucose Missed Detection Rate: High Glucose Alerts	**300**	20.0% (2/10, 6)	20.0% (2/10, 6)	**300**	0.0% (0/10, 6)	10.0% (1/10, 6)	**300**	0.0% (0/10, 6)	10.0% (1/10, 6)
	250	22.2% (4/18, 14)	22.2% (4/18, 14)	**250**	11.1% (2/18, 14)	16.7% (3/18, 14)	**250**	11.1% (2/18, 14)	16.7% (3/18, 14)
	220	7.4% (2/27, 21)	14.8% (4/27, 21)	**220**	3.7% (1/27, 21)	11.1% (3/27, 21)	**220**	3.7% (1/27, 21)	11.1% (3/27, 21)
	180	4.9% (2/41, 26)	4.9% (2/41, 26)	**180**	0.0% (0/41, 26)	0.0% (0/41, 26)	**180**	0.0% (0/41, 26)	0.0% (0/41, 26)

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

Abdomen Sensor Life

After the first successful calibration, 64.3% of sensors worn operated more than six days and up to the full seven days of wear (144 to 168 hours). The mean functional sensor life for sensors worn in the abdomen insertion site over the course of the study was 122.1 hours, with a median functional life of 128.4 hours.

Buttock Insertion Site

Tables 28 and 29 below provide the Guardian sensor values and the percent of data points that fell within 15, 20, 30, 40, and >40 mg/dL or percent of a specific CM glucose range when the sensor worn in the buttocks was calibrated every 12 hours after: Days 1, 3, and 7; Day 1 only, respectively.

Table 28. Agreement (%) of Sensor-CM Paired Points (15/15%- greater than 40/40%) Stratified by Different CM Glucose Ranges, Calibrated every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age, Day Overall

CM Glucose Ranges (mg/dL)	**Number of CGM-CM Pairs**	**Percent of CGM Within 15/15% of CM**	**Percent of CGM Within 20/20% of CM**	**Percent of CGM Within 30/30% of CM**	**Percent of CGM Within 40/40% of CM**	**Percent of CGM Greater Than 40/40% of CM**
Overall	710	84.8	92.3	96.8	98.6	1.4
≥40-60*	7	100	100	100	100	0
>60-80*	34	70.6	79.4	94.1	100	0
>80-180	393	80.9	89.8	94.9	97.5	2.5
>180-300	255	91	96.9	99.6	100	0
>300-350	15	100	100	100	100	0
>350-400	6	100	100	100	100	0

**For glucose ranges ≤ 80 mg/dL, agreement was based on 15/20/30/40 mg/dL. Note: Sensor glucose readings are within 40-400 mg/dL*

Table 29. Agreement (%) of Sensor-CM Paired Points (15/15%- greater than 40/40%) Stratified by Different CM Glucose Ranges, Calibrated every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age, Day 1

CM Glucose Ranges (mg/dL)	**Number of CGM-CM Pairs**	**Percent of CGM Within 15/15% of CM**	**Percent of CGM Within 20/20% of CM**	**Percent of CGM Within 30/30% of CM**	**Percent of CGM Within 40/40% of CM**	**Percent of CGM Greater Than 40/40% of CM**
Overall	335	78.8	87.2	93.7	97	3
>60-80*	19	52.6	63.2	89.5	100	0
>80-180	178	71.9	82.6	89.9	94.4	5.6
>180-300	133	91	96.2	99.2	100	0
>300-350	3	100	100	100	100	0
>350-400	2	100	100	100	100	0

**For glucose ranges ≤ 80 mg/dL, agreement was based on 15/20/30/40 mg/dL. Note: Sensor glucose readings are within 40-400 mg/dL*

The following tables 30 to 33 show the percentage of concurring CGM readings compared to CM values for sensors worn in the buttocks. With ideal performance, the CGM readings would match the CM values. For example, with perfect concurrence, the shaded boxes in the tables below would be 100 percent.

Tables 30 and 31 show the concurrence of the CGM values compared to CM values when calibrating every 12 hours, after Days 1, 3, and 7.

Tables 32 and 33 show the concurrence of the CGM values compared to CM values when calibrating three to four times per day, after Days 1, 3, and 7.

Table 30. Concurrence of CM values and CGM readings using CM glucose ranges; Calibrating every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age, Day Overall

CM Glucose Ranges (mg/dL)	Percent of Matched Pairs-in Each CGM Glucose Range for Each CM Glucose Range											
	CGM (mg/dL)											
	Number of Paired CGM-CM	<40	>=40-60	>60-80	>80-120	>120-160	>160-200	>200-250	>250-300	>300-350	>350-400	>400
>=40-60	11	36.4% (4/11)	63.6% (7/11)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>60-80	37	8.1% (3/37)	24.3% (9/37)	43.2% (16/37)	24.3% (9/37)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>80-120	156	0.6% (1/156)	5.1% (8/156)	9.0% (14/156)	75.6% (118/156)	9.6% (15/156)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>120-160	170	0.0% (0/0)	0.0% (0/0)	2.9% (5/170)	16.5% (28/170)	67.6% (115/170)	12.9% (22/170)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>160-200	144	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	16.0% (23/144)	75.7% (109/144)	8.3% (12/144)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>200-250	130	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	2.3% (3/130)	38.5% (50/130)	56.2% (73/130)	3.1% (4/130)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>250-300	49	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	40.8% (20/49)	53.1% (26/49)	6.1% (3/49)	0.0% (0/0)	0.0% (0/0)

CM Glucose Ranges (mg/dL)	Percent of Matched Pairs-in Each CGM Glucose Range for Each CM Glucose Range											
	CGM (mg/dL)											
	Number of Paired CGM-CM	<40	>=40-60	>60-80	>80-120	>120-160	>160-200	>200-250	>250-300	>300-350	>350-400	>400
>300-350	15	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	33.3% (5/15)	60.0% (9/15)	6.7% (1/15)	0.0% (0/0)
>350-400	6	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	50.0% (3/6)	50.0% (3/6)	0.0% (0/0)

Table 31. Concurrence of CM values and CGM readings using CM glucose ranges; Calibrating three to four times per day, Buttock Insertion Site, Data From Subjects 7-13 Years of Age, Day 1, 3, and 7

	Percent of Matched Pairs-in Each CGM Glucose Range for Each CM Glucose Range											
	CGM (mg/dL)											
CM Glucose Ranges (mg/dL)	Number of Paired CGM-CM	<40	>=40-60	>60-80	>80-120	>120-160	>160-200	>200-250	>250-300	>300-350	>350-400	>400
>=40-60	11	36.4% (4/11)	63.6% (7/11)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>60-80	30	6.7% (2/30)	10.0% (3/30)	50.0% (15/30)	33.3% (10/30)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>80-120	144	0.7% (1/144)	1.4% (2/144)	7.6% (11/144)	80.6% (116/144)	9.7% (14/144)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>120-160	164	0.0% (0/0)	0.0% (0/0)	1.8% (3/164)	16.5% (27/164)	67.1% (110/164)	14.0% (23/164)	0.6% (1/164)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>160-200	140	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	14.3% (20/140)	75.0% (105/140)	10.7% (15/140)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>200-250	127	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	1.6% (2/127)	42.5% (54/127)	51.2% (65/127)	4.7% (6/127)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>250-300	53	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	41.5% (22/53)	39.6% (21/53)	17.0% (9/53)	1.9% (1/53)	0.0% (0/0)

	Percent of Matched Pairs-in Each CGM Glucose Range for Each CM Glucose Range											
	CGM (mg/dL)											
CM Glucose Ranges (mg/dL)	**Number of Paired CGM-CM**	**<40**	**>=40-60**	**>60-80**	**>80-120**	**>120-160**	**>160-200**	**>200-250**	**>250-300**	**>300-350**	**>350-400**	**>400**
>300-350	18	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	38.9% (7/18)	38.9% (7/18)	22.2% (4/18)	0.0% (0/0)
>350-400	6	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	16.7% (1/6)	83.3% (5/6)	0.0% (0/0)

Table 32. Concurrence of CGM readings and CM values using CGM glucose ranges; Calibrating every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age, Day Overall

	Percent of Matched Pairs-in Each CM Glucose Range for Each CGM Glucose Range											
	CM (mg/dL)											
CGM Glucose Ranges (mg/dL)	**Number of Paired CGM-CM**	**<40**	**>=40-60**	**>60-80**	**>80-120**	**>120-160**	**>160-200**	**>200-250**	**>250-300**	**>300-350**	**>350-400**	**>400**
<40	8	0.0% (0/0)	50.0% (4/8)	37.5% (3/8)	12.5% (1/8)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>=40-60	24	0.0% (0/0)	29.2% (7/24)	37.5% (9/24)	33.3% (8/24)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>60-80	35	0.0% (0/0)	0.0% (0/0)	45.7% (16/35)	40.0% (14/35)	14.3% (5/35)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>80-120	155	0.0% (0/0)	0.0% (0/0)	5.8% (9/155)	76.1% (118/155)	18.1% (28/155)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>120-160	156	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	9.6% (15/156)	73.7% (115/156)	14.7% (23/156)	1.9% (3/156)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>160-200	181	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	12.2% (22/181)	60.2% (109/181)	27.6% (50/181)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>200-250	105	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	11.4% (12/105)	69.5% (73/105)	19.0% (20/105)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
>250-300	35	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	11.4% (4/35)	74.3% (26/35)	14.3% (5/35)	0.0% (0/0)	0.0% (0/0)
>300-350	15	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	20.0% (3/15)	60.0% (9/15)	20.0% (3/15)	0.0% (0/0)
>350-400	4	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	25.0% (1/4)	75.0% (3/4)	0.0% (0/0)

Table 33. Concurrence of CGM readings and CM values using CGM glucose ranges; Calibrating three to four times per day, Buttock Insertion Site, Data From Subjects 7-13 Years of Age, Day Overall

	Percent of Matched Pairs-in Each CM Glucose Range for Each CGM Glucose Range											
	CM (mg/dL)											
CGM Glucose Ranges (mg/dL)	**Number of Paired CGM-CM**	**<40**	**>=40-60**	**>60-80**	**>80-120**	**>120-160**	**>160-200**	**>200-250**	**>250-300**	**>300-350**	**>350-400**	**>400**
A) <40	7	0.0% (0/0)	57.1% (4/7)	28.6% (2/7)	14.3% (1/7)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
B) >=40-60	12	0.0% (0/0)	58.3% (7/12)	25.0% (3/12)	16.7% (2/12)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
C) >60-80	29	0.0% (0/0)	0.0% (0/0)	51.7% (15/29)	37.9% (11/29)	10.3% (3/29)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
D) >80-120	153	0.0% (0/0)	0.0% (0/0)	6.5% (10/153)	75.8% (116/153)	17.6% (27/153)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
E) >120-160	146	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	9.6% (14/146)	75.3% (110/146)	13.7% (20/146)	1.4% (2/146)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
F) >160-200	182	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	12.6% (23/182)	57.7% (105/182)	29.7% (54/182)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
G) >200-250	103	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	1.0% (1/103)	14.6% (15/103)	63.1% (65/103)	21.4% (22/103)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)
H) >250-300	34	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	17.6% (6/34)	61.8% (21/34)	20.6% (7/34)	0.0% (0/0)	0.0% (0/0)
I) >300-350	17	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	52.9% (9/17)	41.2% (7/17)	5.9% (1/17)	0.0% (0/0)
J) >350-400	10	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	0.0% (0/0)	10.0% (1/10)	40.0% (4/10)	50.0% (5/10)	0.0% (0/0)

Table 34 below provides data representing sensor accuracy in the buttocks over specific glucose rates of change. The concurrence tables below provide the percent of matched CM pairs to CGM values over specific glucose rates of change for sensors worn in the buttocks calibrated every 12 hours and three to four times per day, respectively.

Table 34. Calibration every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

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	35	37.1% (13/35)	45.7% (16/35)	17.1% (6/35)	0.0% (0/35)	0.0% (0/35)	0.0% (0/35)
[-2, -1)	83	7.2% (6/83)	31.3% (26/83)	59.0% (49/83)	2.4% (2/83)	0.0% (0/83)	0.0% (0/83)
[-1, 0)	272	0.0% (0/272)	4.8% (13/272)	69.9% (190/272)	21.7% (59/272)	2.9% (8/272)	0.7% (2/272)
[0, 1]	199	0.0% (0/199)	0.5% (1/199)	22.1% (44/199)	60.8% (121/199)	15.6% (31/199)	1.0% (2/199)
(1, 2]	97	0.0% (0/97)	0.0% (0/97)	4.1% (4/97)	36.1% (35/97)	54.6% (53/97)	5.2% (5/97)
>2	23	0.0% (0/23)	0.0% (0/23)	0.0% (0/23)	26.1% (6/23)	34.8% (8/23)	39.1% (9/23)

Tables 35 and 36 below provide the Guardian sensor values and the percent difference with respect to comparator method (CM) values when the sensor worn in the buttocks was calibrated every 12 hours and three to four times per day, respectively.

Table 35. CGM Difference to CM within CM Glucose Ranges, Calibrating Every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

CM Glucose Ranges (mg/dL)	Number of Subjects	Number of Paired CGM-CM Pairs	Mean Absolute Percent Difference (%)	Median Absolute Percent Difference (%)
Overall	29	710	9.14	6.92
40-60*	2	7	5.43	5.45
61-80*	10	34	10.85	6.75
81-180	26	393	9.63	6.4
181-300	24	255	7.92	7.21
301-350	4	15	4.64	4.45
351-400	2	6	5.05	4.63

**For glucose ranges ≤ 80 mg/dL, the differences in mg/dL are included instead of percent difference (%). Note: Sensor glucose readings are within 40-400 mg/dL.*

Table 36. CGM Difference to CM within CM Glucose Ranges, Calibrating three to four times per day, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

CM Glucose Ranges (mg/dL)	Number of Subjects	Number of Paired CGM-CM Pairs	Mean Absolute Percent Difference (%)	Median Absolute Percent Difference (%)
Overall	28	686	8.79	6.88
40-60*	2	7	3.61	3.1
61-80*	9	28	7.86	6.2
81-180	25	374	8.99	6.29
181-300	22	253	8.56	7.4
301-350	4	18	7.67	6.91
351-400	2	6	3.01	2.1

**For glucose ranges ≤ 80 mg/dL, the differences in mg/dL are included instead of percent difference (%). Note: Sensor glucose readings are within 40-400 mg/dL.*

Table 37 shows sensor stability in the buttocks by comparing the CM values collected during frequent sample testing days 1, 3, and 7 to their paired sensor points. The tables stratify the paired CM-sensor data by 15/15, 20/20, 30/30, 40/40 and >40/40 mg/dL and percent, respectively.

Table 37. Sensor Stability (accuracy over time) for Calibration every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

Day of Wear	Number of Paired System CM	Mean absolute percent difference (%)	Median absolute percent difference (%)	Percent within 15/15% CM	Percent within 20/20% CM	Percent within 30/30% CM	Percent within 40/40% CM	Percent greater than 40/40% CM
1	335	10.9	7.4	78.8	87.2	93.7	97.0	3.0
3	176	8.5	7.9	86.4	97.2	99.4	100.0	0.0
7	199	6.8	5.2	93.5	96.5	99.5	100.0	0.0

Tables 38 and 39 below provide the number and percentage of CM measurements collected while the continuous glucose monitor read 'low' (< 40 mg/dL), or 'high' (> 400 mg/dL) for sensors worn in the buttocks calibrated every 12 hours.

Table 38. The Number and Percentage of CM values collected when CGM readings displayed 'Low' (less than 40 mg/dL); calibrating every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

CGM Readings	CGM-CM pairs	<55	<60	<70	<80	>80	Total
'LOW'	Cumulative, n	3	4	7	7	1	8
	Cumulative %	38%	50%	88%	88%	13%	

Table 39. The Number and Percentage of CM values collected when CGM readings displayed 'High' (more than 400 mg/dL); calibrating every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

CGM Readings	CGM-CM pairs	>340	>320	>280	>240	<240	Total
'HIGH'	Cumulative, n	0	0	0	0	0	0
	Cumulative %	0%	0%	0%	0%	0%	

Pump Alert Performance using the Buttock Sensor Insertion Site

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

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. 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 40. Glucose TRUE Alert Performance, Calibrating every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			Predictive Only			Threshold &		
	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)
Glucose True Alert Rate: Low glucose Alerts	**50**	25.0% (1/4, 4)	25.0% (1/4, 4)	**50**	11.1% (1/9, 7)	11.1% (1/9, 7)	**50**	16.7% (2/12, 7)	16.7% (2/12, 7)
	55	50.0% (3/6, 4)	50.0% (3/6, 4)	**55**	33.3% (3/9, 7)	22.2% (2/9, 7)	**55**	40.0% (6/15, 7)	33.3% (5/15, 7)
	60	60.0% (3/5, 4)	60.0% (3/5, 4)	**60**	25.0% (3/12, 9)	16.7% (2/12, 9)	**60**	35.3% (6/17, 9)	29.4% (5/17, 9)
	70	60.0% (6/10, 8)	60.0% (6/10, 8)	**70**	36.8% (7/19,	26.3% (5/19, 12)	**70**	40.7% (11/27,	33.3% (9/27, 12)
	80	61.1% (11/18, 12)	61.1% (11/18, 12)	**80**	46.2% (12/26,	38.5% (10/26,	**80**	51.2% (22/43,	46.5% (20/43,
	90	70.8% (17/24, 14)	70.8% (17/24, 14)	**90**	58.3% (21/36,	44.4% (16/36,	**90**	62.5% (35/56,	53.6% (30/56,
Glucose True Alert Rate: High glucose Alerts	**300**	57.1% (4/7, 5)	57.1% (4/7, 5)	**300**	31.3% (5/16,	31.3% (5/16, 11)	**300**	38.1% (8/21,	38.1% (8/21, 11)
	250	73.3% (11/15, 11)	73.3% (11/15, 11)	**250**	41.2% (14/34,	35.3% (12/34,	**250**	50.0% (23/46,	45.7% (21/46,
	220	75.0% (21/28, 19)	75.0% (21/28, 19)	**220**	51.0% (25/49,	49.0% (24/49,	**220**	58.3% (42/72,	56.9% (41/72,
	180	83.3% (40/48, 27)	81.3% (39/48, 27)	**180**	64.3% (45/70,	62.9% (44/70,	**180**	70.6% (77/109,	68.8% (75/109,

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

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); or
- 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); or

- 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 41. Glucose FALSE Alert Performance, Calibrating every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			**Predictive Only**			**Threshold & Predictive**		
	mg/dL	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**
Glucose False Alert Rate: Low Glucose Alerts	**50**	75.0% (3/4, 4)	75.0% (3/4, 4)	**50**	88.9% (8/9, 7)	88.9% (8/9, 7)	**50**	83.3% (10/12, 7)	83.3% (10/12, 7)
	55	50.0% (3/6, 4)	50.0% (3/6, 4)	**55**	66.7% (6/9, 7)	77.8% (7/9, 7)	**55**	60.0% (9/15, 7)	66.7% (10/15, 7)
	60	40.0% (2/5, 4)	40.0% (2/5, 4)	**60**	75.0% (9/12, 9)	83.3% (10/12, 9)	**60**	64.7% (11/17, 9)	70.6% (12/17, 9)
	70	40.0%	40.0%	**70**	63.2%	73.7%	**70**	59.3%	66.7%

	Threshold Only			Predictive Only			Threshold & Predictive		
	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)
		(4/10, 8)	(4/10, 8)		(12/19, 12)	(14/19, 12)		(16/27, 12)	(18/27, 12)
	80	38.9% (7/18, 12)	38.9% (7/18, 12)	**80**	53.8% (14/26, 16)	61.5% (16/26, 16)	**80**	48.8% (21/43, 16)	53.5% (23/43, 16)
	90	29.2% (7/24, 14)	29.2% (7/24, 14)	**90**	41.7% (15/36, 21)	55.6% (20/36, 21)	**90**	37.5% (21/56, 21)	46.4% (26/56, 21)
Glucose False Alert Rate: High Glucose Alerts	**300**	42.9% (3/7, 5)	42.9% (3/7, 5)	**300**	68.8% (11/16, 11)	68.8% (11/16, 11)	**300**	61.9% (13/21, 11)	61.9% (13/21, 11)
	250	26.7% (4/15, 11)	26.7% (4/15, 11)	**250**	58.8% (20/34, 23)	64.7% (22/34, 23)	**250**	50.0% (23/46, 23)	54.3% (25/46, 23)
	220	25.0% (7/28, 19)	25.0% (7/28, 19)	**220**	49.0% (24/49, 26)	51.0% (25/49, 26)	**220**	41.7% (30/72, 26)	43.1% (31/72, 26)
	180	16.7% (8/48, 27)	18.8% (9/48, 27)	**180**	35.7% (25/70, 29)	37.1% (26/70, 29)	**180**	29.4% (32/109, 29)	31.2% (34/109, 29)

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

Table 42. Glucose FALSE Alert Performance, Calibrating three to four times per day, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			Predictive Only			Threshold & Predictive		
	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)
Glucose False Alert Rate: Low Glucose Alerts	**50**	66.7% (2/3, 3)	66.7% (2/3, 3)	**50**	85.7% (6/7, 6)	85.7% (6/7, 6)	**50**	80.0% (8/10, 6)	80.0% (8/10, 6)
	55	25.0% (1/4, 3)	25.0% (1/4, 3)	**55**	62.5% (5/8, 6)	75.0% (6/8, 6)	**55**	50.0% (6/12, 6)	58.3% (7/12, 6)
	60	25.0%	25.0%	**60**	72.7%	81.8%	**60**	60.0%	66.7%

	Threshold Only			Predictive Only			Threshold & Predictive		
	mg/dL	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**
		(1/4, 3)	(1/4, 3)		(8/11, 8)	(9/11, 8)		(9/15, 8)	(10/15, 8)
	70	44.4% (4/9, 7)	44.4% (4/9, 7)	**70**	60.0% (9/15, 11)	73.3% (11/15, 11)	**70**	59.1% (13/22, 11)	68.2% (15/22, 11)
	80	40.0% (6/15, 10)	40.0% (6/15, 10)	**80**	54.2% (13/24, 15)	62.5% (15/24, 15)	**80**	50.0% (19/38, 15)	55.3% (21/38, 15)
	90	30.4% (7/23, 14)	30.4% (7/23, 14)	**90**	36.4% (12/33, 20)	54.5% (18/33, 20)	**90**	34.6% (18/52, 20)	46.2% (24/52, 20)
Glucose False Alert Rate: High Glucose Alerts	**300**	50.0% (3/6, 4)	50.0% (3/6, 4)	**300**	66.7% (10/15, 12)	66.7% (10/15, 12)	**300**	63.2% (12/19, 12)	63.2% (12/19, 12)
	250	21.4% (3/14, 11)	21.4% (3/14, 11)	**250**	54.3% (19/35, 22)	60.0% (21/35, 22)	**250**	46.8% (22/47, 22)	51.1% (24/47, 22)
	220	29.6% (8/27, 18)	29.6% (8/27, 18)	**220**	51.0% (25/49, 25)	53.1% (26/49, 25)	**220**	45.7% (32/70, 25)	47.1% (33/70, 25)
	180	17.8% (8/45, 26)	20.0% (9/45, 26)	**180**	34.8% (23/66, 27)	36.4% (24/66, 27)	**180**	29.7% (30/101, 27)	31.7% (32/101,

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

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 43. Glucose Correct Detection Alert Performance, Calibrating every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			Predictive Only			Threshold & Predictive		
	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)
Glucose Correct Detection Rate: Low Glucose Alerts	**50**	100.0% (1/1, 1)	100.0% (1/1, 1)	**50**	100.0% (1/1, 1)	100.0% (1/1, 1)	**50**	100.0% (1/1, 1)	100.0% (1/1, 1)
	55	100.0% (3/3, 3)	100.0% (3/3, 3)	**55**	100.0% (3/3, 3)	66.7% (2/3, 3)	**55**	100.0% (3/3, 3)	100.0% (3/3, 3)
	60	100.0% (3/3, 3)	100.0% (3/3, 3)	**60**	100.0% (3/3, 3)	66.7% (2/3, 3)	**60**	100.0% (3/3, 3)	100.0% (3/3, 3)
	70	85.7% (6/7, 7)	85.7% (6/7, 7)	**70**	85.7% (6/7, 7)	71.4% (5/7, 7)	**70**	85.7% (6/7, 7)	85.7% (6/7, 7)
	80	85.7% (12/14, 11)	85.7% (12/14, 11)	**80**	85.7% (12/14, 11)	78.6% (11/14, 11)	**80**	85.7% (12/14, 11)	85.7% (12/14, 11)
	90	86.4% (19/22, 16)	86.4% (19/22, 16)	**90**	90.9% (20/22, 16)	72.7% (16/22, 16)	**90**	95.5% (21/22, 16)	86.4% (19/22, 16)
Glucose Correct Detection Rate: High Glucose Alerts	**300**	60.0% (3/5, 4)	60.0% (3/5, 4)	**300**	100.0% (5/5, 4)	100.0% (5/5, 4)	**300**	100.0% (5/5, 4)	100.0% (5/5, 4)
	250	68.8% (11/16, 11)	62.5% (10/16, 11)	**250**	100.0% (16/16, 11)	93.8% (15/16, 11)	**250**	100.0% (16/16, 11)	100.0% (16/16, 11)
	220	95.7% (22/23, 17)	95.7% (22/23, 17)	**220**	100.0% (23/23, 17)	95.7% (22/23, 17)	**220**	100.0% (23/23, 17)	100.0% (23/23, 17)
	180	97.5% (39/40, 24)	95.0% (38/40, 24)	**180**	100.0% (40/40, 24)	100.0% (40/40, 24)	**180**	100.0% (40/40, 24)	100.0% (40/40, 24)

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

Table 44. Glucose Correct Detection Alert Performance, Calibrating three to four times per day, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			Predictive Only			Threshold & Predictive		
	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)
Glucose Correct Detection Rate: Low Glucose Alerts	**50**	100.0% (1/1, 1)	100.0% (1/1, 1)	**50**	100.0% (1/1, 1)	100.0% (1/1, 1)	**50**	100.0% (1/1, 1)	100.0% (1/1, 1)
	55	100.0% (3/3, 3)	100.0% (3/3, 3)	**55**	100.0% (3/3, 3)	66.7% (2/3, 3)	**55**	100.0% (3/3, 3)	100.0% (3/3, 3)
	60	100.0% (3/3, 3)	100.0% (3/3, 3)	**60**	100.0% (3/3, 3)	66.7% (2/3, 3)	**60**	100.0% (3/3, 3)	100.0% (3/3, 3)
	70	83.3% (5/6, 6)	83.3% (5/6, 6)	**70**	83.3% (5/6, 6)	66.7% (4/6, 6)	**70**	83.3% (5/6, 6)	83.3% (5/6, 6)
	80	75.0% (9/12, 10)	75.0% (9/12, 10)	**80**	83.3% (10/12, 10)	75.0% (9/12, 10)	**80**	83.3% (10/12, 10)	83.3% (10/12, 10)
	90	85.0% (17/20, 15)	85.0% (17/20, 15)	**90**	95.0% (19/20, 15)	70.0% (14/20, 15)	**90**	95.0% (19/20, 15)	85.0% (17/20, 15)
Glucose Correct Detection Rate: High Glucose Alerts	**300**	66.7% (4/6, 4)	66.7% (4/6, 4)	**300**	100.0% (6/6, 4)	100.0% (6/6, 4)	**300**	100.0% (6/6, 4)	100.0% (6/6, 4)
	250	70.6% (12/17, 11)	70.6% (12/17, 11)	**250**	100.0% (17/17, 11)	88.2% (15/17, 11)	**250**	100.0% (17/17, 11)	94.1% (16/17, 11)
	220	90.9% (20/22, 16)	90.9% (20/22, 16)	**220**	95.5% (21/22, 16)	95.5% (21/22, 16)	**220**	95.5% (21/22, 16)	95.5% (21/22, 16)
	180	97.4% (37/38, 22)	94.7% (36/38, 22)	**180**	100.0% (38/38, 22)	100.0% (38/38, 22)	**180**	100.0% (38/38, 22)	100.0% (38/38, 22)

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

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 45. Glucose Missed Detection Alert Performance, Calibrating every 12 hours, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			**Predictive Only**			**Threshold & Predictive**		
	mg/dL	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**	**mg/dL**	**±30 Min (n/N of Events, # of Subject)**	**±15 Min (n/N of Events, # of Subject)**
Glucose Missed Detection Rate: Low Glucose Alerts	**50**	0.0% (0/1, 1)	0.0% (0/1, 1)	**50**	0.0% (0/1, 1)	0.0% (0/1, 1)	**50**	0.0% (0/1, 1)	0.0% (0/1, 1)
	55	0.0% (0/3, 3)	0.0% (0/3, 3)	**55**	0.0% (0/3, 3)	33.3% (1/3, 3)	**55**	0.0% (0/3, 3)	0.0% (0/3, 3)
	60	0.0% (0/3, 3)	0.0% (0/3, 3)	**60**	0.0% (0/3, 3)	33.3% (1/3, 3)	**60**	0.0% (0/3, 3)	0.0% (0/3, 3)
	70	14.3% (1/7, 7)	14.3% (1/7, 7)	**70**	14.3% (1/7, 7)	28.6% (2/7, 7)	**70**	14.3% (1/7, 7)	14.3% (1/7, 7)
	80	14.3% (2/14, 11)	14.3% (2/14, 11)	**80**	14.3% (2/14, 11)	21.4% (3/14, 11)	**80**	14.3% (2/14, 11)	14.3% (2/14, 11)
	90	13.6% (3/22, 16)	13.6% (3/22, 16)	**90**	9.1% (2/22, 16)	27.3% (6/22, 16)	**90**	4.5% (1/22, 16)	13.6% (3/22, 16)
Glucose Missed Detection Rate: High Glucose Alerts	**300**	40.0% (2/5, 4)	40.0% (2/5, 4)	**300**	0.0% (0/5, 4)	0.0% (0/5, 4)	**300**	0.0% (0/5, 4)	0.0% (0/5, 4)
	250	31.3% (5/16, 11)	37.5% (6/16, 11)	**250**	0.0% (0/16, 11)	6.3% (1/16, 11)	**250**	0.0% (0/16, 11)	0.0% (0/16, 11)
	220	4.3% (1/23, 17)	4.3% (1/23, 17)	**220**	0.0% (0/23, 17)	4.3% (1/23, 17)	**220**	0.0% (0/23, 17)	0.0% (0/23, 17)
	180	2.5% (1/40, 24)	5.0% (2/40, 24)	**180**	0.0% (0/40, 24)	0.0% (0/40, 24)	**180**	0.0% (0/40, 24)	0.0% (0/40, 24)

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

Table 46. Glucose Missed Detection Alert Performance, Calibrating three to four times per day, Buttock Insertion Site, Data From Subjects 7-13 Years of Age

	Threshold Only			Predictive Only			Threshold & Predictive		
	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)	mg/dL	±30 Min (n/N of Events, # of Subject)	±15 Min (n/N of Events, # of Subject)
Glucose Missed Detection Rate: Low Glucose Alerts	**50**	0.0% (0/1, 1)	0.0% (0/1, 1)	**50**	0.0% (0/1, 1)	0.0% (0/1, 1)	**50**	0.0% (0/1, 1)	0.0% (0/1, 1)
	55	0.0% (0/3, 3)	0.0% (0/3, 3)	**55**	0.0% (0/3, 3)	33.3% (1/3, 3)	**55**	0.0% (0/3, 3)	0.0% (0/3, 3)
	60	0.0% (0/3, 3)	0.0% (0/3, 3)	**60**	0.0% (0/3, 3)	33.3% (1/3, 3)	**60**	0.0% (0/3, 3)	0.0% (0/3, 3)
	70	16.7% (1/6, 6)	16.7% (1/6, 6)	**70**	16.7% (1/6, 6)	33.3% (2/6, 6)	**70**	16.7% (1/6, 6)	16.7% (1/6, 6)
	80	25.0% (3/12, 10)	25.0% (3/12, 10)	**80**	16.7% (2/12, 10)	25.0% (3/12, 10)	**80**	16.7% (2/12, 10)	16.7% (2/12, 10)
	90	15.0% (3/20, 15)	15.0% (3/20, 15)	**90**	5.0% (1/20, 15)	30.0% (6/20, 15)	**90**	5.0% (1/20, 15)	15.0% (3/20, 15)
Glucose Missed Detection Rate: High Glucose Alerts	**300**	33.3% (2/6, 4)	33.3% (2/6, 4)	**300**	0.0% (0/6, 4)	0.0% (0/6, 4)	**300**	0.0% (0/6, 4)	0.0% (0/6, 4)
	250	29.4% (5/17, 11)	29.4% (5/17, 11)	**250**	0.0% (0/17, 11)	11.8% (2/17, 11)	**250**	0.0% (0/17, 11)	5.9% (1/17, 11)
	220	9.1% (2/22, 16)	9.1% (2/22, 16)	**220**	4.5% (1/22, 16)	4.5% (1/22, 16)	**220**	4.5% (1/22, 16)	4.5% (1/22, 16)
	180	2.6% (1/38, 22)	5.3% (2/38, 22)	**180**	0.0% (0/38, 22)	0.0% (0/38, 22)	**180**	0.0% (0/38, 22)	0.0% (0/38, 22)

Note: Given the small sample size of data available in the low range, the alert performance in the 50 mg/dL and 60 mg/dL should be interpreted with caution and may not reflect actual use performance

Buttock Sensor Life

After the first successful calibration, 81.3% of sensors worn operated more than six days and up to the full seven days of wear (144 to 168 hours). The mean functional sensor life for sensors worn in the buttock insertion site over the course of the study was 142.7 hours, with a median functional life of 158.1 hours.

Precision Analysis

Precision of the System was evaluated by comparing the results from two separate sensors worn on the same subject at the same time.

Data from two sensors worn at the same time for 11 subjects in the abdomen/abdomen insertion locations provided 772 pairs of CGM Measurements, with a mean Percent Absolute Relative Difference (PARD) during the study 7.83% with a coefficient of variation (%CV) of 5.7%.

Data from two sensors worn at the same time for 18 subjects in the abdomen/buttock insertions location provided 1302 pairs of CGM Measurements, with a mean Percent Absolute Relative Difference (PARD) during the study 11.33% with a coefficient of variation (%CV) of 7.8%.

Data from two sensors worn at the same time for 10 subjects in the buttock/buttock insertions location provided 695 pairs of CGM Measurements, with a mean Percent Absolute Relative Difference (PARD) during the study 10.93% with a coefficient of variation (%CV) of 8.1%.

3. Sub Group Analysis
   Guardian sensor performance and 670G System performance was evaluated withinstudy population subgroups, such as age, gender, ethnicity, body mass index (BMI), baseline HbA1c, prior CGM experience, and exercise activity (during in-clinic portions of the study).

   Although the studies were not powered for analysis of subpopulations, no significant differences in performance were noted based on these subgroup analyses. However,it should be noted that the system was not evaluated in pump naïve users.

4. Pediatric Extrapolation
   In this premarket application, existing clinical data was not leveraged to support approval of ta pediatric patient population.

I. 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 pivotal clinical study included (hybrid closed loop pediatric study (G150247)) included 9 principal investigators. The sensor performance study (G120262, the Guardian Sensor (3) study) included 11 principal investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Continued Access Study

Subjects in the HCL pediatric pivotal study were given the opportunity to extend the use of their 670G systems study devices for a period of up to 2 years after the end of the study period or until the device is available commercially (if approved). During the continued access period, subjects were scheduled to come in for office visits every 3 months. At each of the quarterly visits, subjects were asked about the occurrence of adverse events and device complaints. The purpose of the continued access study was to obtain additional safety information regarding the device.

The data provided for the continued access study was collected through November 17, 2017. The continued access study is currently ongoing.

One hundred two (102) subjects opted to participate in the continued access phase of the study. As of November 17, 2017, four subjects withdrew from the study because the pump did not fit their lifestyle and one subject was withdrawn for not wearing the sensor.

There were a total of 200 adverse events reported through November 17, 2017 for the 7-13 year age group in the continued access study. Of these 200 adverse events, 81 events were reported to be device related. The majority (127) of adverse events during the continued access study involved severe hyperglycemia. Of the 127 severe hyperglycemia events reported, 67 events were device related (see Table 47 below) and 14 were from other device-related events (i.e., rash, scratch, abscess, skin infections, hyperglycemia, and skin erythema). For all 127 severe hyperglycemia events, no hospital or ER visits were noted. and all resolved without sequelae.

Table 47: Device Related Severe Hyperglycemia Events

Cause	Total
changed infusion set and blood glucose improved	18
occlusion alarm	9
safe basal	3
bent cannula	1

Cause	Total
not identified reason (monitoring ongoing since time of data base lock)	16
infusion set came out	6
infusion set came apart	1
power loss error	1
changed infusion set and blood glucose improved & safe basal	5
infusion set pulled out halfway	1
blue guard was left on needle	1
power error 25	3
kinked infusion set	2
TOTAL	**67**

There were two episodes of severe hypoglycemia and two serious adverse events reported during the continued access phase. None of these events were device related. All of these events resolved without sequalae and were not noted to be associated with ER visits or hospitalizations. One of the severe hypoglycemia events was reported to be due to incorrect insulin bolus, and was classified as moderate severity. The other severe hypoglycemia event was reported to have occurred while the subject was not wearing the CGM and not in Auto Mode, and was classified as a serious adverse event. The other serious adverse event was reported to be a fracture of the radius and ulna due to a fall, and was not device related.

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 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 clinical study was not designed to evaluate clinical effectiveness endpoints (e.g., reduction of hypoglycemia, etc.), and only observational information about safety and effectiveness of device function (insulin delivery) were collected.

The results of the clinical studies performed to support this submission establish a reasonable assurance of effectiveness that the MiniMed 670G System can automatically adjust basal insulin rates 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 the delivery of insulin

when used as intended, as an adjunct to blood glucose testing in subjects with type 1 diabetes mellitus.

The effectiveness of the Guardian sensor component was based on the performance

evaluation of the Guardian Sensor compared to the blood glucose values measured by the CM during in-clinic sessions spanning the wear period of the sensor (7 days). The performance data presented above (Tables 12 to 46) established the sensor performance across the claimed measuring range (40 to 400 mg/dL glucose), the precision, and the calibration frequency (calibrate minimally every 12 hours or 3-4 times a day) of the 7 day wear period for the Guardian sensor. The performance data presented above also established the performance of the alarms and alerts of the Guardian sensor. It should be noted that although the accuracy study is small, the pediatric HCL study and its continuation phase provides additional performance information for the sensor specifically in the context of use within the 670G System.

The results of the clinical studies performed to support approval establish a reasonable assurance that the MiniMed 670G system is effective for its 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)

A higher incidence of severe hyperglycemia was reported during the pediatric HCL study (and continuation phase to date) compared with the 14 years and above age group. It is possible that the 7-13 year age group could have a higher risk of severe hyperglycemia compared to the 14 years and above population.

Based on the data provided, it is possible that the reported alert performance for the 7-13 year age group could result in an increased risk of hypoglycemia in the 7-13 year age group, compared to the 14 years and above population.

Sensor breakage with fragments retained under the skin is a potential adverse event related to use of the CGM component of the 670G system, but this was not observed during these studies. Based on postmarket experience with similar devices and the results observed in these clinical studies, 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, and the results observed in these clinical studies, 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 continuous glucose sensor readings (together with blood glucose meter readings) are used by the 670G System to determine automated insulin delivery, including insulin suspension and insulin dosing, and are the basis for alerts for hypoglycemia and hyperglycemia. The continuous glucose sensor readings are also to be used by the patient for tracking and trending, when in Manual Mode. While in manual mode, the continuous glucose sensor 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.

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 670G system in some cases (i.e., decline to take additional bolus of insulin as recommended by the 670G system in setting of falsely high continuous glucose reading or exit Auto Mode).

The results of the clinical studies performed and described in section IX and X above to support approval establish a reasonable assurance that the MiniMed 670G system is safe for its intended use.

C. Benefit-Risk Determination

Summary of Benefits:

The probable benefits of the device are based on data collected in clinical studies conducted to support PMA approval as described above in Sections IX and X.

The MiniMed 670G System is a novel device in 7 to 13 year olds, which features in addition to sensor-augmented insulin pump therapy; an automated insulin delivery (Auto Mode) feature, aswell as a predictive low glucose management feature ('Suspend before low'). Compared to therun-in period for the pivotal study, results from the pivotal study period demonstrated the following:

- Suggested a potential for improvement in overall glycemic control based on change in HbA1c values between run-in and the study phase.
- Less time and number of events with sensor glucose <70 mg/dL, particularly overnight.
- Less time and number of events with sensor glucose >250 mg/dL in tables
- More time with sensor glucose in the 70-180 range.
- Improved quality of life and good usability of the device based on Human Factors Studies

The 670G System is intended for user-specified continuous delivery of basal insulin and insulin boluses for the management of Type 1 diabetes mellitus in persons 7 years of age and older. In the 670G System, insulin delivery is coupled with the continuous monitoring and trending of glucose levels in the fluid under the skin. The MiniMed 670G System can be programmed to automatically suspend insulin delivery for up to two hours when the sensor glucose value falls below a predefined or predicted threshold value. The MiniMed 670G System can be programmed to automatically calculate the insulin dose, based on information received from the CGM, to achieve glycemic control throughout the day and night. The Auto Mode and insulin suspend features described above can be enabled on the 670G system, but they cannot be enabled at the same time. The Guardian CGM is intended to supplement self-monitoring of blood glucose to track and trend interstitial glucose levels as estimates of glucose excursions in the blood. The adjustable hypoglycemia and hyperglycemia alerts are intended to warn the patients that they need to test their blood glucose to see if they need to take action to treat or prevent a hypoglycemic or hyperglycemic event. Furthermore, CGM measurements, which are performed every 5 minutes for 7 days via an indwelling sensor, provide tracking and trending information to supplement blood glucose meter measurements that are made several times daily and for calibration of the CGM device.

The use of the continuous glucose monitor gives patients and healthcare providers glucose tracking and trending information not feasible using traditional blood glucose monitoring as blood glucose meters only provide information about discrete, intermittent blood glucose levels. Patients and healthcare providers can review the tracking and trending data by day and time of day such as daytime, or night time when fewer fingersticks are usually performed. The CGM includes a software package to aid in the evaluation of glucose trends over several days to detect patterns which may indicate a need to adjust therapy such as changes to basal rates and bolus dose instructions.

Furthermore, the continuous glucose monitors provide real time knowledge of interstitial glucose levels that can be displayed on the insulin pump screen. The system can be set to provide notifications based on sensor trends or threshold, adding information unavailable by traditional discrete monitoring.

Interstitial glucose trending information can be used to provide rate of change alerts that notify the patient that interstitial glucose is increasing or decreasing at a rate that raises concern for hyperglycemia or hypoglycemia. Threshold and Predictive ('suspend on low' and 'suspend before low' respectively) alert settings allow for high alerts, low alerts, and alerts regarding insulin delivery suspension. With the guidance of their healthcare provider the patient can set predictive or threshold high or low alerts to provide notifications that sensor glucose is approaching (the case of the predictive) or has reached (in the case of the threshold) level of concern. These alerts and alarms are especially helpful for individuals with hypoglycemia unawareness (these individuals may develop severe hypoglycemia with loss of consciousness, seizures, or rarely death without the normal warning symptoms), or during the night when patients may have prolonged hypoglycemia that does not awaken them and could proceed to severe hypoglycemia if not treated in time. Traditional blood glucose testing is not able to automatically alert users to these potentially dangerous episodes of asymptomatic hypoglycemia.

The PLGM feature is an optional tool (not available when the Auto Mode of the670G is activated), which when activated, is intended to suspend insulin delivery (for up to 2 hours) when the sensor glucose value is predicted to reach a preset value between 50 to 90 mg/dL. The PLGM feature also resumes insulin delivery based on feedback from the CGM system after 2 hours or before based on a pre-set glucose value. The user has the option to choose between suspending on a sensor glucose threshold ('suspend on low') or suspending based on a prediction ('suspend before low').

The ability to automatically suspend insulin when the user is unaware of and/or unable to treat a low blood sugar with carbohydrate is a desirable feature given the risk of severe hypoglycemia and its potential complications (seizures, unconsciousness and death). The ability to automatically resume insulin is also a desired feature as it reduces the risk of hyperglycemia, ketoacidosis and DKA from prolonged insulin suspension. The degree of prevention of hypoglycemia could not be determined in the predictive suspend study because of the limitations of study design. Nevertheless, if used as intended and not as the primary method for preventing hypoglycemia, the predictive suspend feature is likely to provide more benefit than risk.

The Auto Mode feature is a new optional tool to automate insulin delivery within the MiniMed 670G system. The automated insulin delivery is based on sensor glucose readings. There is no automated insulin-delivery system currently commercially available. Auto Mode, when activated, will calculate the insulin dose at five minute intervals, based on CGM data, in order to achieve a target glucose threshold (120 mg/dL) throughout the day and night. Meal boluses are the responsibility of the user. Blood glucose meter readings will be used for any correction boluses, as well as when the user elects to take a reading prior to their meal bolus (while in Auto Mode).

There are several different options (Modes) within Auto Mode:
(1) Temp Target - The user can set a temporary target glucose of 150 mg/dL for a period of time within "Temp Target" mode
(2) Safe Basal Mode (or Safe Basal Low Mode) - The Auto Mode algorithm initiates a "safe basal mode" or "safe basal low" when the safeguards within the system algorithm determine that either the sensor data is not adequate for Auto Mode (sensor under-reading or no sensor data), or delivery at the minimum or maximum limit for a set amount of time has elapsed. The Auto Mode algorithm will determine when to deliver safe basal or safe basal low, depending on the patient's sensor glucose value. The various safe basal rates are defined as:

- Safe basal is the calculated rate of insulin [U/h] that will bring the fasting blood glucose to the value of 120 [mg/dL].
- Safe Basal Low is the calculated rate of insulin [U/h] that will bring the fasting blood glucose to the value of 200 [mg/dL].

The ability to automate insulin delivery (Auto Mode feature) is a desirable feature given the risk of severe hypoglycemia and DKA associated with insulin pump therapy, especially when patients are unable to adjust insulin doses or monitor their blood glucose (e.g., when sleeping). In addition, automated insulin delivery has the potential to be convenient to the user. Both the clinical and patient communities have expressed a strong desire for an automated insulin delivery system ("artificial pancreas") to be commercially available in the US.

The 670G insulin pump has the potential to be used as a traditional insulin pump as well as an automated insulin delivery system. Benefits of insulin therapy with continuous insulin infusion include the ability to:

1. Administer insulin frequently without repeated injections;
2. Set multiple basal rates during the day to better match basal insulin requirements which may fluctuate during the course of the day;
3. Calculate active insulin remaining from previous boluses to avoid "insulin stacking", which can lead to hypoglycemia;
4. Administer bolus doses over an extended time;
5. Use a "built in" calculation tool to assist users in calculating appropriate bolus insulin doses for meals based on current blood glucose levels, anticipated number of carbohydrates to be consumed, target blood glucose levels, insulin sensitivity, insulin to carbohydrate ratio, and active insulin time, factors which

are determined by users' experiences and diabetes care providers' recommendations/instructions.

Summary of Risks:

Risks of the Auto Mode feature include the following:

- The insulin pump may inappropriately suspend or decrease insulin delivery due to software error or erroneous CGM data.
- The insulin pump may inappropriately increase insulin delivery or suggest that the user administer additional insulin due to software error or erroneous CGM data.
- Hyperglycemia and ketosis from automatic insulin suspension or decrease in insulin delivery.
- Hypoglycemia from automatic increase in insulin delivery.
- Hyperglycemia, ketosis, ketoacidosis, hypoglycemia due to willing or unwilling off label use of the device.
- Inappropriate use of Auto Mode can result in an increased risk of the above risks

Risks of the predictive suspend feature include the following:

- The predictive suspend feature may inappropriately suspend insulin due to a software defect or erroneous CGM data, which inaccurately detects impending hypoglycemia or a threshold glucose
- The predictive suspend feature may inappropriately resume insulin due to a software defect or erroneous CGM data, which inaccurately detects resolution of hypoglycemia or a threshold glucose
- The predictive suspend feature may not appropriately suspend insulin due to a software defect or erroneous CGM data, which does not detect impending hypoglycemia or a threshold glucose.
- The predictive suspend feature may not appropriately resume insulin due to a software defect or erroneous CGM data, which does not detect resolution of hypoglycemia or a threshold glucose
- Hyperglycemia and ketosis from automatic insulin suspension.
- Inappropriate reliance on predictive suspend feature can result in an increased risk of the above risks.

Risks of the pump hardware problems include the following:

- Hypoglycemia from excessive pump delivery due to a hardware defect
- Hyperglycemia and ketosis possibly leading to ketoacidosis due to inappropriate insulin suspension or pump failure resulting in cessation of all insulin delivery due to either a hardware defect or software anomaly.

Risks of the CGM include:

- Sensor error resulting in incorrect tracking and trending or threshold detection; increased false negative and false positive low threshold alerts and alarms or high threshold alerts, and incorrect rate of change calculations that could adversely affect

treatment decisions, and result in an increased risk of hypoglycemia or hyperglycemia

- Non-adjunctive use of CGM data for meal bolusing decisions could result in an increased risk of hypoglycemia or hyperglycemia
- 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
    - Hematoma
    - Unnecessary fingersticks
    - Hyperglycemia following insulin suspensions
    - Ketosis following insulin suspensions
    - Sensor may break leaving a sensor fragment under the skin

- Potential device-related serious adverse events include:
    - DKA resulting from suspension of insulin delivery or inadequate insulin delivery (which can result from catheter occlusion, hardware or software malfunction, or erroneous CGM readings),
    - Severe hypoglycemia resulting from over-delivery of insulin (which can result from hardware or software malfunction or erroneous CGM readings), which may lead to seizure, unconsciousness, and rarely, death

A higher incidence of severe hyperglycemia was reported during the pediatric HCL study (and continuation phase to date) compared with the 14 years and above age group. The majority of these reported severe hyperglycemia events were mild in intensity, and none of these events of severe hyperglycemia were reported to have progressed to DKA. Although use of Auto Mode was associated with reduced exposure to high sensor glucose values (compared with the run-in phase) during this study, it may be possible that the 7-13 year age group could have a higher risk of severe hyperglycemia compared to the 14 years and above age group. This potential increased risk is adequately mitigated through information in the labeling, fixed alarms for high sensor glucose, as well as the availability of real-time sensor glucose information. Further, additional surveillance will be conducted in the postmarket setting for the pediatric population for severe hyperglycemia rates.

Based on the data provided relating to sensor performance, it is possible that the reported alert performance for the low sensor glucose ranges in the 7-13 year age group could result in an increased risk of hypoglycemia in the 7-13 year age group, compared to the 14 years and above population. There were no device related severe

hypoglycemia events reported during the HCL pivotal study as well as the continuation phase of the HCL pivotal study. Further, use of Auto Mode was associated with reduced exposure to low sensor glucose values (compared with run-in phase) during this study. This potential risk is adequately mitigated through warnings and other information in the labeling relating to the alert performance, and the availability of real-time sensor glucose information. Further, additional surveillance relating to the low sensor glucose alerts, will be conducted in the postmarket setting.

Summary of Other Factors:

- Hypoglycemia can cause serious morbidity and mortality
- The fear and risk of hypoglycemia limits the treatment of hyperglycemia
- Intensive insulin therapy is well known to increase the risk of hypoglycemia
- Optimizing glucose control is well known to decrease the risk of chronic complications of diabetes mellitus, which result in significant morbidity and mortality

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 making with their health care providers on lifestyle changes and treatment decisions. Patients have also expressed in personal 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 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 670G system, as discussed above, outweigh the risks.

XIV. CDRH DECISION

CDRH issued an approval order on June 21, 2018. The final conditions of approval cited in the approval order are described below.

In addition to the Annual Report requirements, the applicant must provide the following data in post-approval study (PAS). The Multi-Center, Randomized, Parallel, Adaptive, Controlled Trial in Adult and Pediatric patients with Type 1 Diabetes Using Hybrid Closed Loop System and Control (CSII, MDI, and SAP) at Home is a 6 month, multi-

center, randomized, parallel, adaptive study in adult and pediatric subjects ages 2-80 years with type 1 diabetes with a 6 month continuation period. Up to 1500 subjects will be enrolled in order to have 1120 subjects who enter the study period. Up to 70 investigational centers in the US and Canada, as well as in the Medtronic EMEA region, that is comprised of Europe, the Middle East and Africa, will be enrolled. The purpose of this study is to demonstrate the safety and effectiveness of the Hybrid Closed Loop system (HCL) in adult and pediatric patients with type 1 diabetes in the home setting. The study population will have a large range for duration of diabetes and glycemic control, as measured by glycosylated hemoglobin (A1C). Follow-up visits are scheduled throughout the study period up to 6 months and throughout the continuation period up to 6 months. Safety endpoints include Diabetic Ketoacidosis, severe hyperglycemia, severe hypoglycemia, serious adverse events, and unanticipated adverse device effects.

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.

V. REFERENCES

None.