SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Artificial Pancreas Device System, Threshold Suspend

Device Trade Name: MiniMed 630G System with SmartGuard

Device Procode: OZO, MDS, NBW, LFR

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

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P150001

Date of FDA Notice of Approval: August 10, 2016

Priority Review: *Not Applicable*

II. INDICATIONS FOR USE

MiniMed 630G System with SmartGuard
The MiniMed 630G System with SmartGuard™ is intended for continuous delivery of basal insulin (at user selected rates) and administration of insulin boluses (in user selectable amounts) for the management of diabetes mellitus in persons, sixteen 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 630G system includes SmartGuard™, which can be programmed to temporarily suspend delivery of insulin for up to two hours when the sensor glucose value falls below a predefined threshold value.

The MiniMed 630G System with SmartGuard™ consists of the following devices: MiniMed 630G Insulin Pump, Enlite® Sensor, One-press serter, Guardian® Link Transmitter System, CareLink® USB, Bayer's CONTOUR ® NEXT LINK 2.4 Wireless Meter, and Bayer's CONTOUR® NEXT Test Strips. The system requires a prescription.

The MiniMed 630G System with SmartGuard™ is 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 MiniMed 630G system.

The MiniMed 630G System with SmartGuard™ is not intended to be used directly for preventing or treating hypoglycemia but to suspend insulin delivery when the user is unable to respond to the SmartGuard™ Suspend on low alarm to take measures to prevent or treat hypoglycemia themselves. Therapy to prevent or treat hypoglycemia should be administered according to the recommendations of the user's healthcare provider.

Enlite® Sensor
The Enlite® Sensor is intended for use with Medtronic MiniMed Insulin pump (MMT-1715). It continuously monitors glucose levels in persons with diabetes.

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

Guardian® Link Transmitter System
The Medtronic MiniMed Guardian Link Transmitter System is indicated for use as a component of select Medtronic continuous glucose monitoring and sensor-enabled pump systems. It processes, stores and transmits glucose sensor values to data collection and display devices. The Guardian Link Transmitter System is not intended to function as a stand-alone device and is for single-patient use. The Guardian Link Transmitter System includes the Guardian Link Transmitter (MMT-7763), charger (MMT-7715), watertight tester (MMT-7726), and One-press serter (MMT-7512).

CareLink® USB
The Medtronic CareLink® USB is indicated for use by patients at home, and clinicians in a medical office setting, to facilitate communication between MiniMed 630G insulin pump and a personal computer. The computer must use Medtronic diabetic therapy management software.

Bayer CONTOUR® NEXT Link 2.4 Wireless Blood Glucose Glucose Monitoring System
The CONTOUR® NEXT Link 2.4 Wireless Blood Glucose Monitoring System is an over the counter (OTC) and/or prescription device utilized by persons with diabetes in home settings for the measurement of glucose in whole blood, and is for single-patient use only. The CONTOUR® NEXT Link 2.4 wireless blood glucose monitoring system is indicated for use with fresh capillary whole blood samples (drawn from the fingertip or palm only). The CONTOUR® NEXT Link 2.4 Blood Glucose Meter can wirelessly connect to the MiniMed 630G pump through the use of radio frequency communication. The meter can transmit glucose values, be used as a remote control to facilitate delivery of a bolus of insulin from the insulin pump, and facilitate transfer of information from the pump to the Medtronic MiniMed data management software. The CONTOUR® NEXT Link 2.4 Wireless Blood Glucose Monitoring System is not intended for the diagnosis of or screening for diabetes mellitus and is not intended for use on neonates.

III. CONTRAINDICATIONS

The MiniMed 630G System with SmartGuard user guide contains the following contraindications:

- Pump therapy is not recommended for people who are unwilling or unable to perform a minimum of four blood glucose tests per day.

- 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.

IV. WARNINGS AND PRECAUTIONS

The MiniMed 630G System with Smart Guard user guide contains the following warning:

> *The Suspend on low featurecauses the pump to temporarily suspend insulin delivery for two hours when the sensor glucose reaches a set limit. Under some conditions of use, the pump can suspend again, resulting in limited insulin delivery. Prolonged suspension can increase the risk of serious hyperglycemia, ketosis and ketoacidosis.*

Additional warnings and precautions can be found in the MiniMed 630G System with SmartGuard labeling.

V. DEVICE DESCRIPTION

The MiniMed 630G System with SmartGuard is comprised of the following devices:

MiniMed 630G Insulin Pump

The MiniMed 630G Insulin Pump is an ambulatory, battery operated, rate-programmable infusion pump designed to deliver insulin from a reservoir. The reservoir is driven by a motor to deliver patient determined basal rate profiles and patient selected bolus amounts of insulin into the subcutaneous tissue through an FDA-cleared infusion set.

The MiniMed 630G Insulin Pump is offered as model MMT-1715. This model uses a 3.0 mL insulin reservoir, and displays blood-glucose (BG) units in mg/dL. The device does not offer users the option to change unit measures.

The MiniMed 630G shares a similar mechanical pump design with the Minimed 530G system, and both pumps use the same threshold suspend control algorithm. The major difference between the hardware of the two pumps is the use of a color screen and updated button interface in the 630G.

The MiniMed 630G Insulin Pump is designed to receive and display real-time glucose values received from the provided transmitter. Enlite sensor signals are transmitted from the transmitter to the MiniMed 630G Insulin Pump via RF telemetry and converted into glucose concentrations based on calibration values from either the included Bayer Contour blood

glucose meters, or commercially available blood glucose meters. Signals are updated and transmitted to the pump every five minutes.

The real time sensor glucose values, displayed by the MiniMed 630G Insulin Pump, are not intended to be used directly for making therapy adjustments. The patient 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 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 630G Insulin Pump.

The MiniMed 630G System with SmartGuard uses the same Threshold Suspend system as the MiniMed 530G system. This tool provides the patient the means to set the pump to temporarily suspend insulin delivery automatically for up to two hours when the sensor glucose level is equal to or less than a selected threshold. The patient has the capability to select a 'Threshold Suspend' threshold within the 60 mg/dL to 90 mg/dL range. When the 'Threshold Suspend' tool is set to 'ON,' the system compares the sensor glucose value to the programmed Suspend threshold whenever the sensor glucose value is updated (every five minutes). When the sensor glucose value is below the set threshold, a user-defined alarm occurs and the patient may elect to continue or cancel the temporary pump suspension of insulin delivery. If the user does not respond to the initial alarm within a preset time, an emergency siren alarm is sounded and insulin is suspended.

The use of the Threshold Suspend tool is optional and the patient can turn the tool 'ON' and 'OFF'.

If the user does not respond to the alarm or siren, the pump will automatically suspend for two hours. At the end of the two hours, insulin delivery will resume and the system will be unable to suspend the pump automatically for four hours post-insulin resumption even if the sensor glucose value is below the threshold.

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 user-defined alarm will then re-sound, followed by a siren if not acknowledged, and the pump will suspend (unless canceled by the user). The interval between the cancellation of the Threshold Suspend and the next possible threshold alarm will be the duration of the patient's specified Low Alert Repeat (5-60 minutes).

If the patient responds to the alarm or siren by electing to accept the insulin suspension, the pump will suspend. At the end of the two hours, the pump will resume insulin delivery until the next sensor glucose value is below the set threshold suspend value. The interval between the accepted Threshold Suspend and the next possible threshold alarm will be the duration of the patient's specified Low Alert Repeat (5-60 minutes). This means that it is possible for the system to suspend insulin delivery for two hours, followed by a minimal amount of insulin delivery (5 minutes), and re-suspend insulin delivery for two more hours. This loop can be continued for as long as the patient acknowledges the pump suspension (by electing to continue) and the sensor value remains below the set threshold value.

The patient can cancel the temporary pump suspension at any time during the two-hour period regardless if the suspension occurred because he/she was not able to respond to the initial alarm or he/she accepted the suspension.

The MiniMed 630G Insulin Pump is capable of storing 90 days of pump history and glucose sensor data. The pump has a graphical display that the patient 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.

Enlite Glucose Sensor (MMT-7008)

The Enlite sensor is a single-use, disposable component, which is intended for use with MiniMed 630G Insulin Pump to continuously monitor glucose levels. It is inserted into the subcutaneous tissue of the patient and connected to a transmitter device, the Guardian Link Transmitter System (model MMT-7772). The sensor/tube assembly is flexible and has a small cross-section designed to minimize pain and discomfort during use. A rigid introducer needle aids in the insertion of the sensor into the subcutaneous tissue, and retracts into the polycarbonate hub after use. This is intended to prevent accidental needle sticks and allows for safe disposal once the sensor is in place. The sensor/base assembly connects to the transmitter, which in turn communicates with the 630G insulin pump. The Enlite Sensor is intended to be worn for up to six days.

Enlite Serter (MMT-7510)

The Enlite Serter was designed for aiding in the insertion of the Enlite Sensor. It is intended to be used by a patient or a clinician to introduce the sensor into the subcutaneous tissue at a fixed depth, with minimal discomfort and technique dependency, and with minimal exposure of the sensor needle.

Guardian Link Transmitter System:

The Guardian Link Transmitter System consists of the Guardian Link Transmitter (model MMT-7726), Charger (model MMT-7715), and Watertight Tester (model MMT-7726).

The Guardian Link Transmitter provides power to the sensor and measures the sensor signal current (I_{SIG}). The I_{SIG} is an electrical current level that is proportional to the glucose level in the subcutaneous interstitial fluid of the patient. The I_{SIG} is converted to a digital signal, and is filtered to reduce noise artifact. The digital signal is then transmitted to a receiving device through RF link once every 5 minutes. The Guardian Link Transmitter is intended to provide the patient with the convenience of viewing real-time glucose values that can be analyzed to track patterns and improve overall diabetes management. Real-time glucose values are not intended to be used directly for making therapy adjustment, but rather to provide an indication that unplanned finger stick with a home blood glucose monitor may be needed.

Accessories:

The following accessories are compatible with the MiniMed 630G System with SmartGuard:

Reservoirs and Infusion Sets	
Paradigm Reservoir	MMT-326A, MMT-332A
MiniMed Mio Infusion Set	MMT-921, MMT-923, MMT-925, MMT-941, MMT-943, MMT-945, MMT-965, MMT-975
MiniMed Silhouette Infusion Set	MMT-368, MMT-369, MMT-370, MMT-377, MMT-378, MMT-381, MMT-382, MMT-383, MMT-384
MiniMed Sure-T Infusion Set	MMT-862, MMT-864, MMT-866, MMT-874, MMT-876, MMT-886
MiniMed Quick Set Infusion Set	MMT-386, MMT-387, MMT-394, MMT-396, MMT-397
Paradigm Polyfin Infusion Set	MMT-312S, MMT-312L
Paradigm Sof-Set Infusion Set	MMT-317, MMT-318, MMT-324, MMT-325
Meter	
Bayer Contour NEXT LINK 2.4 Meter	MMT-1352, MMT-1152
RF Communication Devices	
CareLink USB	MMT-7306

Bayer Contour NEXT LINK 2.4 Glucose Meter:
The Bayer CONTOUR NEXT LINK 2.4 Wireless Blood Glucose Monitoring System can directly communicate with the MiniMed 630G System with SmartGuard. It consists of a small handheld electronic device, dry reagent strips and liquid controls to be used for the measurement of glucose in capillary whole blood by persons with diabetes. Blood glucose results are displayed in the meter window and stored in the meter's memory. The COUNTOUR NEXT LINK meter also contains RF functions to send Blood Glucose Meter results to the MiniMed 630G System with SmartGuard, to program an insulin bolus from the pump, and facilitate transfer of data to the CareLink therapy-management software.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Control of diabetes can be achieved through a combination of methods and behaviors. Self behaviors include healthy eating, taking the clinically indicated medications, and being active. Persons with diabetes may also administer insulin by injection or by using other insulin infusion pumps as prescribed by his/her physician. Methods of controlling glucose levels (glycemic control) have been shown to reduce severe diabetes-related complications. Methods of monitoring glycemic control include periodic measurement of Hemoglobin A_{1c} (HbA_{1c}), 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 patients and their healthcare providers to monitor the effectiveness of glycemic control and make more immediate treatment modifications.

There are similar insulin pumps and combined pump-CGM systems currently on the market from this sponsor and other sponsors. Each alternative method for monitoring glycemic

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

VII. MARKETING HISTORY

The Minimed 630G System with SmartGuard has not been marketed in the United States. But a similar insulin pump system (the MiniMed 530G System) has been in commercial distribution in the United States since 2013. The Enlite Sensor (MMT-7008) has been in commercial distribution in the United States since 2013, and in the European Union since 2011. These devices have not been withdrawn from marketing for any reason due to safety and effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g. complications) associated with the use of the device.

The following events are possible adverse device effects of inserting a sensor into 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. Reported sensor breakage rate with similar devices has been very low, however, and this study was not powered or designed to assess the rate of breakage. No sensor breakage was documented in the clinical studies supporting approval of this device.There were no reports of subject death, unanticipated adverse device effect (UADE), diabetic ketoacidosis, or serious adverse events related to the device or study procedure during any of the clinical studies (G110044, G110131/A001 and G100028).

There are additional risks due to missed alerts and false negative hypoglycemic and hyperglycemic readings related to patients not being alerted to the need to perform a fingerstick to detect hypoglycemia or hyperglycemia. Additionally, there is a risk associated with false alerts and false positive hypoglycemia and hyperglycemia readings related to the need to perform unnecessary fingersticks to confirm an erroneous low or high reading. Patients who only use blood glucose meters to manage their diabetes without the aid of a CGM would also be unaware of the need to perform additional testing to detect an abnormal blood sugar (unless they were exhibiting symptoms of an abnormal blood glucose).

The risks of inaccurate Enlite sensor glucose results is not unreasonably higher than the risk of managing diabetes with a blood glucose meter alone and these include 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. However, if the patient relies on sensor glucose values and does not perform fingerstick blood glucose tests as recommended (4-7 times daily) the risks of CGM use increases; especially if the sensor error results in failure to detect glucose out of the target glucose range (failure of Low and High alerts) or incorrect insulin dosing.

Inaccurate calculation of the rate of change of interstitial glucose by the CGM could result in failure to identify trends of increasing or decreasing glucose and alerts to the patient that an unplanned blood glucose check should be performed. Rate of change detection errors result in the patient losing the opportunity to perform additional blood glucose tests and take appropriate measures to stop a trend of increasing or decreasing glucose levels that could lead to serious hypoglycemia or hyperglycemia. Inaccurate calculation of the rate of change of glucose could also lead to unnecessary additional blood glucose tests. As discussed above the risk of using sensor rate of change information for making treatment decisions, rather than as a prompt for unplanned blood glucose checks, increases the risk of CGM use.

There are risks associated with using the Threshold Suspend tool. As with the sensor based alerts, the threshold alarm is subject to sensor errors that can result in missed hypoglycemia and no pump suspension, or inappropriate pump suspension when blood glucose is above the sensor suspend threshold (suspension in the absence of hypoglycemia) potentially resulting in hyperglycemia and ketosis. Under certain conditions of use after the initial 2-hour suspension the pump will resume insulin delivery but can re-suspend after a short period of time (as little as 5-minutes) rather than after 4 hours. Repeated pump suspensions, especially if the initial suspension was in error, increases the risk of more severe hyperglycemia, ketosis, and possibly DKA. Patients using insulin pumps can manually suspend insulin or set a temporary basal rate of zero at any time, which can also result in hyperglycemia, ketosis, and possibly DKA if the interruption of insulin delivery is prolonged. Data from the ASPIRE study (IDE # G110044/S002) suggested that the use of the Threshold Suspend feature may potentially worsen glycemic control. Increased incidences of blood and urine ketones were observed in the Threshold Suspend group as compared to the Control group. When ketone levels were reported, the mean blood ketone concentration was higher in the Threshold Suspend group than in the Control group. In addition, more patients in the Threshold Suspend group reported positive ketone values when they exhibited symptoms (nausea, vomiting or abdominal pain). These hyperglycemia risks might be further amplified in patients with worse baseline control compared to those enrolled in the ASPIRE study. The risks of the Threshold Suspend tool can be mitigated if patients do not rely on the tool for treating or mitigating hypoglycemia if they are aware of Low Alerts or Threshold Suspend alarms, perform blood glucose checks, and treat hypoglycemia as instructed by their healthcare providers. Patients should also not rely on the sensor to detect hypoglycemia and perform blood glucose checks in response to symptoms of hypoglycemia. These risks were evaluated during the review of the MiniMed 530G System (PMA # P120010/S046). See the Summary of Safety and Effectiveness Data for the MiniMed 530G for additional information.

Risks of pump hardware problems include the following: possible hypoglycemia from over-delivery of insulin due to a hardware defect, as well as hyperglycemia and ketosis possibly leading to ketoacidosis due to inappropriate insulin suspension, occlusion of the infusion set, or pump failure resulting in cessation of all insulin delivery due to either a hardware defect or software anomaly

IX. SUMMARY OF PRECLINICAL STUDIES

A summary of the non-clinical laboratory studies that were performed on the MiniMed 630G System with SmartGuard is provided below. New testing was not performed on those

components that are identical to those of the MiniMed 530G System (P120010). These identical components include the insulin reservoir, the adhesive patch used to attach the transmitter to a subject, the CGM sensor and sensor tube, and the sensor insertion device (the Enlite 1-Press Serter). Testing on these devices was reviewed under P120010. See the SSED for P120010 for descriptions of the non-clinical testing performed on these components of the system.

A. Laboratory Studies

Non-clinical testing was performed on the 640G insulin pump (MMT-1712)[1], Guardian Link Transmitter (MMT-7763A), and the 640G system as a whole including the Bayer NEXT LINK 2.4 meter (MMT-1152 and MMT-1352). Nonclinical studies focused on bench testing to support compliance with component and system requirement specifications and testing of hardware requirements and mechanical requirements.

MMT-1712 Insulin Pumps

Twenty-nine MMT-1712 pumps were subjected to the following functional and environmental tests to ensure that these devices will continue to function normally even when exposed to extreme environmental conditions:

Test	Purpose	Acceptance Criteria Summary
Basal Delivery Volume Accuracy	Demonstrate accuracy of pumps to deliver minimum (0.025 U/hr), intermediate (1.0 U/hr), mid (6.0 U/hr), and max (35 U/hr) basal rate	Error percentages for hourly intervals within ±5%. Cumulative error within ±10%.
Max/Min Bolus Accuracy	Demonstrate accuracy of pumps to deliver maximum and minimum bolus volumes at the following volume and delivery speed settings: - 75U, 6 U/hr - 75U, 15 U/min - 0.025U, 6 U/hr - 0.1U, 6 U/hr	The error percentage of the mean for all bolus deliveries meets system requirements.
Occlusion Sensitivity	Demonstrate ability of system to detect the presence of an occlusion during normal use and notify the user at standard delivery rate (6U/hr) and quick delivery rate (15 U/min)	The pump detects an occlusion and notifies user with an alarm within 5 units of delivered insulin. No ruptures or leaks are caused by the occlusion.
Occlusion alarm during priming	Demonstrate ability of system to detect the presence of an occlusion during priming and notify the user.	The pump detects an occlusion during priming procedure and notifies the user with an alarm. No

1 The MiniMed 630G Insulin Pump (MMT-1715) shares identical hardware with the 640G (MMT-1712). The only difference between the two systems is in the APDS algorithm. The Agency considers hardware testing of either system to be equivalent.

Test	Purpose	Acceptance Criteria Summary
		ruptures or leaks caused by the occlusion.
Chemical Compatibilitiy	Demonstrate the ability of various pump components (external case, labels, keypad overlay, LCD, and internal reservoir compartment) to withstand exposure to the following chemicals for between 45 seconds – 1 minute: U100 Insulin (Humalog or Novolog), a solution of 1 part dish detergent to 9 parts water, 70% Isopropyl Alcohol.	The pump is not visibly damaged (no signs of cracking, crazing, or melting to the unaided eye), and functions properly as determined by the accurate delivery of a bolus programmed using the keypad and display. Pumps pass general functional testing and maintain ±5% delivery accuracy after testing.
Environmental storage conditions	Pumps demonstrate the ability to withstand storage conditions of -20 to 50 ºC with 5-95% relative humidity.	The pump is not visibly damaged, and functions properly as determined by the accurate delivery of a bolus programmed using the keypad and display. Pumps pass general functional testing and maintain ±5% delivery accuracy after testing.
Temperature shock test	For pumps, demonstrate the ability to maintain basic safety when undergoing rapid changes in temperature exposure: 10 cycles from -20 to 60 ºC at 10 ºC/minute, with 30-minute dwell times at each plateau.	Pumps pass general functional testing and maintain ±5% delivery accuracy if delivery continues. Any cessation in delivery must be accompanied by an alarm.
Operating environment conditions	Pumps demonstrate the ability to operate with temperature of 5 to 40 ºC, 20-90% relative humidity, and 7.4-15.4 psiA atmospheric pressure.	Pump is not visibly damaged. The keypad, display and motor drive function properly as determined by the accurate delivery of a bolus programmed using the keypad and display. Pumps must pass general functional testing and maintain ±5% delivery accuracy after testing.
Random vibration test per EN 60601-2-24	Pumps demonstrate reliable operation under home use vibration conditions: 3-8 Hz with 7.5 mm displacement, and 8-300 Hz with 2 g acceleration peak value. Vibration exposures tested in 3 orthogonal axes.	Pump is not visibly damaged. The keypad, display and motor drive function properly as determined by the accurate delivery of a bolus programmed using the keypad and display. Pumps pass general functional testing and maintain ±5% delivery accuracy after

Test	Purpose	Acceptance Criteria Summary
		testing.
Drop test per EN 60601-2-24	Demonstrate safe operation after six repeated 1 meter drops onto 50 mm thick hardwood – one drop for each of 6 device faces or axes (±X, Y, Z)	Pump maintains delivery accuracy of ±5% if delivery continues. Any cessation in delivery must be accompanied by an alarm.
Button activation force	Demonstrate that the force required to activate the user interface buttons on the pump is 5 ± 1N	Button activation force of 5 ± 1N.
Push test per EN 60601-1	Demonstrate that when subjected to expected external forces, pumps maintain basic safety and/or essential performance.	When subjected to a steady force of 17lbf, the pump passes a general functional test and maintains delivery accuracy ±5%. When subjected to a steady force greater than 17lbf, the pump maintains basic safety: any cessation in insulin delivery must be accompanied by an alarm.
Mold stress relief per EN 60601-1	Demonstrate that after release of any internal stresses due to the plastic molding process, the pump maintains basic safety.	After exposure to 70ºC for 7 hours, and return to room temperature, any cessation in delivery by the pump must be accompanied by an alarm.
Pump Internal Battery Testing	Demonstrate that the internal battery in the pump is capable of lasting for the 4 year life of the pump.	After simulated 4 years of aging, pumps meet original specifications regarding battery life: pumps provide a warning 10±2 hours prior to cessation of delivery due to battery depletion, and an audible and visible warning 30 +2/-0 minutes before cessation (and continuously visible, intermittent audible alerts thereafter until cessation). At least 3 minutes before end of battery life the pump shall stop delivery and maintain an audible and visible alarm for the duration of the battery capacity.
Magnetic field detection algorithm	Demonstrate that the pump can maintain basic safety in the presence of magnetic field strong enough to influence its operation.	The pump alarms before the pump slide is displaced a distance equivalent to the delivery of 1 unit of U100 insulin (0.0035 inches)

Test	Purpose	Acceptance Criteria Summary
Audio alarm test per EN 60601-2-24	Demonstrate that the audio alarm levels are sufficiently loud	The audible alarm produces a sound pressure level of at least 50 dBA at 1 meter distance.
Fluid ingress per IPX8	Demonstrate reliable operation of the pump when submerged to a depth of 12ft in water for 24 hours	Pumps pass general functional testing and maintain ±5% delivery accuracy. Any cessation of delivery is accompanied by an alarm. Pumps have not gained an excess of 0.1g or more, and liquid water is not visibly present.
Fluid ingress per IPX4	Demonstrate reliable operation of pump when exposed to splashing water.	Pumps pass general functional testing and maintain ±5% delivery accuracy. Any cessation of delivery must be accompanied by an alarm. No visual indication of water ingress.
Simulated Shipping test per ASTM D4169-09	Demonstrate reliable operation of pumps after shipping conditions	All labels and barcodes are legible and intact. Pumps must pass general functional testing and maintain ±5% delivery accuracy after testing.
Electrostatic Discharge Susceptibility (ESD) per EN60601-1-2	Demonstrate reliable operation of pump when exposure to ESD in an environment with 30-60% relative humidity.	For indirect contact discharge, the pump maintains essential performance to levels of ±2, 4, and 6 kV. The pump maintains basic safety to levels of ±8kV. For direct air discharge, the pump maintains essential performance to levels of ±2, 4, and 8kV. The pump maintains basic safety to levels of ±15 and 22kV. Cessation of delivery must be accompanied by an alarm.
ESD Susceptibility – Internal MiniMed requirement	Demonstrate reliable operation of pump when exposure to ESD in an environment with 1-5% relative humidity.	For direct air discharge, the pump maintains basic safety when exposed to ±15, 22, and 30kV. Cessation of delivery must be accompanied by an alarm.
EMC/EMI Testing per EN 60601-1-2:2007	Demonstrate ability of the pump to operate in environments with EMI which meet the standard of EN 60601-1-2:2007	Maintain basic safety and essential performance during exposure to EMI – delivery accuracy must meet specification. BG Meter

Test	Purpose	Acceptance Criteria Summary
		commanded bolus amount matches pump displayed delivered amount.

All protocols and acceptance criteria have been reviewed and found to be acceptable. All pump devices met all pre-determined acceptance criteria during this testing.

Guardian Link Transmitter (MMT-7763A)

Twenty-nine Guardian Link transmitters (MMT-7763A) were subjected to the following functional and environmental tests to ensure that these devices will continue to function normally when exposed to extreme environmental conditions.

Test	Purpose	Acceptance Criteria
Chemical Compatibilitiy	Demonstrate the ability of various components to withstand exposure to the following chemicals for between 45 seconds – 1 minute: U100 Insulin (Humalog or Novolog), a solution of 1 part dish detergent to 9 parts water, 70% Isopropyl Alcohol.	No cracks, crazing, dissolving or discoloration to the transmitter surface.
Environmental storage conditions	Transmitters withstand -25 to 55ºC, 10-100% relative humidity.	No visible degradation. When connected to a simulated sensor, signal current is 53.5 nA ±10%. Leak rate <0.40 mbar.
Temperature shock test	Transmitters demonstrate reliable performance after 10 cycles from -5 to 45 ºC with 5 minute ramp time and 30 minute dwell time at each plateau.	No visible degradation, and signal current when connected to a simulated sensor is 53.5 nA ±10%. Leak rate <0.40 mbar.
Operating environment conditions	Transmitters demonstrate the ability to operate with temperature of -5-45 ºC, 95% relative humidity, 8.9-15.4 psiA	No visible degradation. Signal current of 53.5 nA ±10%.
Random vibration test per EN 60601-2-24	Transmitters demonstrate reliable operation after exposure to 10-100 Hz @ $(1\ m/s^2)^2$/Hz, 100-200 Hz @ -3dB/octave, and 200-2000 Hz @ 0.5 $(m/s^2)^2$/Hz for 30 minutes in each axis.	No visible degradation, and signal current when attached to simulated sensor is 53.5 nA ±10%.
Drop test per EN 60601-2-24	Demonstrate safe operation after six repeated 1 meter drops onto 50 mm thick hardwood – one drop for each	No visible degradation, and signal current when attached to simulated sensor is 53.5 nA ±10%.

Test	Purpose	Acceptance Criteria
	of 6 device faces or axes (±X, Y, Z)	
Push test per EN 60601-1	Demonstrate that transmitters maintain performance after exposure to applied force.	When subjected to a steady force of 56 lbf ±2.25 lbf, the transmitter shows no sign of distortion or damage.
Mechanical Shock per IEC 60601-1-11	Demonstrate reliable transmitter operation after exposure to 150 m/s^2 (15g) acceleration, with three shocks per axis in each direction (±X, Y, Z) for a total of 18 shocks.	Transmitters show no visible degradation, and signal current when attached to simulated sensor is 53.5 nA ±10%.
Impact Test per IEC 60601-1	Demonstrate ability of transmitter to withstand an impact from a 500g steel ball with approximate diameter of 50mm dropped from a height of 1.3m	Transmitter must not introduce a safety hazard to the patient or other persons in the surroundings.
Connector insertion force	Demonstrate force required to connect battery charger and sensor to transmitter is less than 3 pounds.	Insertion force is less than 3 pounds.
Connector retention force	Demonstrate force required to retain battery charger to transmitter is greater than 0.5 pounds and less than 3 pounds.	Charger retention force is greater than 0.5 pounds and less than 3 pounds.
Connector cycling	Demonstrate that the transmitter can withstand 244 insertion/removal cycles with both the battery charger and the sensor.	Transmitters show no visible degradation, and signal current when attached to simulated sensor is 53.5 nA ±10%.
Mold stress relief per EN 60601-1	Demonstrate that after release of any internal stresses due to the plastic molding process, the transmitter maintains basic safety.	After exposure to 70ºC for 7 hours, transmitters are returned to room temperature and tested for basic safety. No visible damage or distortion.
Fluid ingress per IPX8	Demonstrate reliable operation of the transmitter when submerged to a depth of 8ft for 30 minutes.	No water ingress by visual inspection. Sensor signal of 2.35-2.65 nA in the 2.5 nA range; 24.25-25.75 nA in the 25 nA range; and 145.5-154.5 nA in the 150 nA range.
Protection against solid foreign objects per IP2X and IP4X	Demonstrate that the full diameter of a 12.5mm or 1.0mm spherical probe cannot pass through any opening of the transmitter.	The full diameter of a 12.5mm and 1.0mm spherical probe cannot pass through any opening of the transmitter.

All protocols, test reports, and acceptance criteria were reviewed and found to be acceptable. All transmitter devices met all pre-determined acceptance criteria during this testing.

MiniMed 630G System with SmartGuard

The MiniMed 630G System with SmartGuard will all components operating together, including the Bayer NEXT LINK 2.4 meter (MMT-1152 and MMT-1352), was subjected to the following functional and environmental tests to ensure that these devices will continue to function normally when exposed to extreme environmental conditions:

Test	Purpose	Acceptance Criteria
EMC/EMI Testing per EN 60601-1-2:2007	Demonstrate ability of the system to operate in environments with EMI which meet the standard of EN 60601-1-2:2007	Maintain basic safety and essential performance during exposure to EMI – delivery accuracy within ±5%. BG Meter commanded bolus amount matches pump displayed delivered amount.
Wireless Coexistence	Demonstrate ability of system to withstand expected levels of wireless transmission from other sources	Maintain basic safety and essential performance during exposure to wireless transmission sources – delivery accuracy within ±5%.
FCC and Avionics	Demonstrate compatibility with FCC regulation	Emitted levels must be per FCC CFR 47 Part 15.247. It is acceptable that the pump pay lose RF communication with the transmitter. In this case the pump will alarm “Lost Sensor” to notify the user. Pump operating mode shall not be affected. BG Meter commanded bolus amount matches pump displayed delivered amount. No interruption of pump alarms, and no change in pump operating mode or programmed settings.
X-ray Immunity	Demonstrate reliable operation when exposed to x-ray – 100kV, 100 uA exposure for 2 minutes	Pump history download shows no change in transmitted values. Pump and BG meter maintain association and complete system functionality. BG Meter commanded bolus amount matches pump displayed delivered amount. No interruption of pump alarms, and no change in pump

Test	Purpose	Acceptance Criteria
		operating mode or programmed settings. Sensor signal of 53.5 nA ±10% when connected to a simulated sensor.
RF Performance	Demonstrate reliable system operation when multiple pump/transmitter pairs are operating within close proximity	Less than 10 % packet loss with RF communication between pump and transmitter, and between pump and BG meter. Sensor signal values of 53.5 nA ±10%, and no unexpected lost sensor alerts. BG Meter commanded bolus amount matches pump displayed delivered amount.
Electronic article surveillance immunity	Demonstrate that the system operates reliably when exposed to EMI from electronic article surveillance equipment.	Pump delivery accuracy within ±5%. Sensor signal values of 53.5 nA ±10%. BG Meter commanded bolus amount matches pump displayed delivered amount.
Cell phone and cordless phone immunity	Demonstrate that the system operates reliably when exposed to EMI specifically in common cell phone spectra (800-960 MHz and 1700-2200 MHz @ 1MHz steps) using WCDMA, WCDMA/3GPP, GSM/EDGE, DECT, IS95, PHS, NADC, PDC, and cordless phone spectra (2400 and 900 MHz)	Pump history download shows no change in transmitted values. Pump and BG meter maintain association and complete system functionality. BG Meter commanded bolus amount matches pump displayed delivered amount. No interruption of pump alarms, and no change in pump operating mode or programmed settings.

All protocols, test reports, and acceptance criteria have been reviewed and found to be acceptable. All system components met all pre-determined acceptance criteria during this testing.

The results for all of the above validation testing were found to be acceptable. These results support the conclusion that the MiniMed 630G System with SmartGuard is safe for its intended use.

Biocompatibility Testing

The manufacturer referenced biocompatibility testing from previously approved submissions for the materials that comprise the Enlite Sensor, Enlite Serter, Watertight Tester, and all patient-contacting and insulin-contacting components of the 630G system including the adhesive patch, sensor tube, sensor circuit, and insulin pump reservoir. This information has been evaluated and approved as part of previous submissions. Please see the SSED for P120010 for more information.

Sterility
The manufacturer referenced sterility testing from previous submissions for the Enlite Sensor, Enlite Serter, and Watertight Tester. This information has been evaluated and approved as part of previous submissions. Please see the SSED for P120010 for more information.

Packaging/Shelf-Life
The MiniMed 630G System with SmartGuard and the Guardian Link Transmitter System (MMT-7772) were tested under conditions of simulated shipping per ASTM D4169. Testing included environmental conditioning, manual handling, vehicle stacking, loose load vibration, low pressure testing, vehicle vibration, concentrated impact, and final inspection of samples. The MiniMed 630G Insulin Pump (MMT-1715) has a shelf life of six months based on the internal backup battery, which requires regular recharging. The Guardian Link Transmitter is intended to operate for a period of at least 12 months.

The packaging of the Bayer Contour NEXT Link Meter 2.4 was subject to and has met the requirements for international shipping and handling using procedures and methods defined in ISTA Procedure 2A, *Performance Test Procedure for Individual Packaged Products Weighing 150 Lbs. (68 Kg) or Less*.

The sponsor referenced packaging and shelf life testing from previous submissions for the Enlite Sensor, Enlite Serter, and Watertight Tester. This information has been evaluated and approved as part of previous submissions. Please see the SSED for P120010 for more information.

Software
Comprehensive verification and validation testing was conducted to confirm that the software used in the MiniMed 630G System with SmartGuard meets all specified requirements and that the software will operate reliably and safely under normal or abnormal use conditions.

The software verification and validation were carried out in accordance with the FDA's "General Principles of Software Validation: Final Guidance for Industry and FDA Staff." Software development activities included establishing detailed software requirements, linking requirements with associate verification tests, software code reviews, unit testing, system level testing and defect tracking and dispositioning to ensure the software conforms to patient needs and intended uses.

Human Factors Testing
Formative and summative human factors studies were conducted with the MiniMed 630G System with SmartGuard. The summative study was a non-randomized, multicenter study that was performed using the MiniMed 630G System with SmartGuard and 37 representative participants. The study participants received training that was consistent with the training that patients would receive with the commercial product. Usability evaluations were performed that included critical device tasks and results of the study demonstrated that users understood the instructions provided in the user guide and that they could use the device safely.

B. Animal Studies

None

C. Additional Studies

None

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The manufacturer referenced two clinical studies that are described in the SSED for the MiniMed 530G System (P120010,) and which were used to establish a reasonable assurance of safety and effectiveness of the MiniMed 530G System for its intended use, including the accuracy performance of the Enlite sensor. The in-clinic studies were performed in the United States under IDE # G110131/A001 (Enlite Sensor Accuracy) and G100028 (Threshold Suspend). The sponsor also referenced a third clinical study that is described in the SSED for a panel-track supplement of the 530G System (P120010/S046). Please see the original P120010 SSED and the P120010/S046 SSED (available in the FDA PMA database) for details on these clinical studies, including Study Designs, Safety and Effectiveness Results, and Financial Disclosure information.

A. Study Design for CGM predictive alert setting

A formal clinical study was not performed for the MiniMed 630G System with SmartGuard. The 630G System is similar to the approved 530G System with the exception of a new hardware insulin pump platform and lower overall false alerts (achieved through a modified predictive low alert algorithm). See pre-clinical section above for validation of the insulin pump through non-clinical bench testing which included insulin delivery accuracy, occlusion detection, environmental stress, electromagnetic compatibility, insulin compatibility testing, and human factors testing. The predictive low alert algorithm used in the 630G System was developed using a previously collected clinical study dataset from the IPro2 recorder approval (P980022) and further validated using the previously collected clinical study dataset from the Enlite sensor performance dataset (in IDE# G110131, the same dataset used to support approval of the MiniMed 530G in PMA# P120010). The data from these studies was analyzed post-hoc by the modified predictive alert algorithm and the performance of the algorithm is presented in the table in the Study Results section, below.

B Study Results for CGM predictive alert settings

In the Table below, performance at various CGM alert settings is determined by CGM comparison with YSI within ±30 minutes. A 'hypoglycemic event' is defined as an instance where a subject's true blood glucose level, as measured by YSI, is below the CGM alert setting (i.e. the value in the left-hand column in the table below). 'CGM compared to YSI' reports the percent of times the CGM falls below the CGM alert setting when YSI is below that setting. 'YSI compared to CGM' reports the percent of time the YSI agrees with the CGM alerts.

CGM alert setting (mg/dL)	CGM Compared to YSI		YSI Compared to CGM	
	Hypoglycemic events correctly detected (%)	**Hypoglycemic events not detected (%)**	**Alerts verified by hypoglycemic events (%)**	**False Alerts (%)**
	±30 Min	**±30 Min**	**±30 Min**	**±30 Min**
60	82.9	17.1	58.6	41.4
70	88.3	11.7	75.2	24.8
80	95.6	4.4	79.8	20.2
90	97.5	2.5	83.0	17.0

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

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

The potential benefits and risks of the threshold suspend tool has been publicly discussed in several meetings, including a meeting on Artificial Pancreas Device Systems held in 2010 and co-sponsored by the FDA and the National Institutes of Health.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The MiniMed 630G System with SmartGuard is not intended to be used directly for preventing or treating hypoglycemia but to suspend insulin delivery when the user is unable to respond to the Threshold Suspend alarm.

No additional clinical study was required for the MiniMed 630G System with SmartGuard. The preclinical test data presented above (Section IX) establish a reasonable assurance of safety and effectiveness for the MiniMed 630G System with SmartGuard. The results of the preclinical testing demonstrate that the MiniMed 630G System with SmartGuard complies with the applicable voluntary standards for biocompatibility, sterilization, electromagnetic compatibility, and safety. The device passed all the testing in accordance with the national and international standards. Internal verification and validation testing confirmed that product specifications were met which support the intended use and technological characteristics. The verification and validation of the device software were completed according to the FDA guidance entitled General Principles of Software Validation: Final Guidance for Industry and FDA Staff.

The clinical testing performed in P120010 for the MiniMed 530G System and the preclinical and human factors/usability testing completed on the MiniMed 630G System

with SmartGuard and its components for this PMA support the operation of this device as a system.

Bench testing was conducted to evaluate the modified predictive alert algorithm. The results of this bench testing demonstrated that the predictive alert performance is similar to what was demonstrated in P120010. With respect to the performance demonstrated in P120010, the false positive rate has been decreased slightly, and the false negative rate has been increased slightly. The increased false negative rate does not appear to be clinically significant, and the decrease in false positive rate may encourage broader utilization of this feature by device users.

B. Safety Conclusions

The risks of the device are largely based on testing result for the MiniMed 630G System with SmartGuard, as well as data collected in a clinical study conducted to support PMA approval of the MiniMed 530G System as described in the SSEDs for P120010 and P120010/S046.

The following events are possible adverse device effects of inserting a sensor into the 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.. No sensor breakage was documented in the clinical studies supporting approval of this device. Reported sensor breakage rate with similar devices has been very low, however, and this study was not powered or designed to assess the rate of breakage. There were no reports of subject death, unanticipated adverse device effect (UADE), diabetic ketoacidosis, or serious adverse events related to the device or study procedure during any of the clinical studies (G110044, G110131/A001 and G100028). There are additional risks due to missed alerts and false negative hypoglycemic and hyperglycemic readings related to patients not being alerted to the need to perform a fingerstick to detect hypoglycemia or hyperglycemia. Additionally, there is a risk associated with false alerts and false positive hypoglycemia and hyperglycemia readings related to the need to perform unnecessary fingersticks to confirm an erroneous low or high reading. Patients who only use blood glucose meters to manage their diabetes without the aid of a CGM would also be unaware of the need to perform additional testing to detect an abnormal blood sugar (unless they were exhibiting symptoms of an abnormal blood glucose).

The risks of inaccurate Enlite sensor glucose results (which is not unreasonably higher than the risk of managing diabetes with a blood glucose meter alone) include 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.. However, if the patient relies on sensor glucose values and does not perform fingerstick blood glucose tests as recommended (4-7 times daily) the risks of CGM use increases; especially if the sensor error results in failure to detect glucose out of the target glucose range (failure of Low and High alerts) or incorrect insulin dosing.

Inaccurate calculation of the rate of change of interstitial glucose by the CGM could result in failure to identify trends of increasing or decreasing glucose and alerts to the patient that an unplanned blood glucose check should be performed. Rate of change detection errors result in the patient losing the opportunity to perform additional blood glucose tests and take appropriate measures to stop a trend of increasing or decreasing glucose levels that could lead to serious hypoglycemia or hyperglycemia. Inaccurate calculation of the rate of change of glucose could also lead to unnecessary additional blood glucose tests. As discussed above the risk of using sensor rate of change information for making treatment decisions, rather than as a prompt for unplanned blood glucose checks, increases the risk of CGM use.

There are risks associated with using the Threshold Suspend tool. As with the sensor based alerts, the threshold alarm is subject to sensor errors that can result in missed hypoglycemia and no pump suspension, or inappropriate pump suspension when blood glucose is above the sensor suspend threshold (suspension in the absence of hypoglycemia) potentially resulting in hyperglycemia and ketosis. Under certain conditions of use after the initial 2-hour suspension the pump will resume insulin delivery but can re-suspend after a short period of time (as little as 5-minutes) rather than after 4 hours. Repeated pump suspensions, especially if the initial suspension was in error, increases the risk of more severe hyperglycemia, ketosis, and possibly DKA. Patients using insulin pumps can manually suspend insulin or set a temporary basal rate of zero at any time, which can also result in hyperglycemia, ketosis, and possibly DKA if the interruption of insulin delivery is prolonged.

Data from the ASPIRE study (G110044/S002, P120010/S046) suggested that the use of the Threshold Suspend feature may potentially worsen glycemic control. Increased incidences of blood and urine ketones were observed in the Threshold Suspend group as compared to the Control group. When ketone levels were reported, the mean blood ketone concentration was higher in the Threshold Suspend group than in the Control group. In addition, more patients in the Threshold Suspend group reported positive ketone values when they exhibited symptoms (nausea, vomiting or abdominal pain). These hyperglycemia risks might be further amplified in patients with worse baseline control compared to those enrolled in the ASPIRE study. The risks of the Threshold Suspend tool can be mitigated if patients do not rely on the tool for treating or mitigating hypoglycemia if they are aware of Low Alerts or Threshold Suspend alarms, perform blood glucose checks, and treat hypoglycemia as instructed by their healthcare providers. Patients should also not rely on the sensor to detect hypoglycemia and perform blood glucose checks in response to symptoms of hypoglycemia.

Risks of the pump hardware problems include possible hypoglycemia from over-delivery of insulin due to a hardware defect, as well as 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

C. Benefit-Risk Conclusions

The probable benefits of the device are based on data collected in clinical studies performed on the previous version of this device (MiniMed 530G). The MiniMed 630G System with SmartGuard is similar to the approved 530G System with the exception of a new hardware insulin pump platform and lower overall false alerts (modified predictive low alert algorithm). The predictive low alert algorithm used in the MiniMed 630G was developed using the clinical study dataset in the IPro2 recorder approval (P980022) and further validated using the clinical study data in the Enlite sensor performance dataset (in G110131). The MiniMed 630G System with SmartGuard utilizes the same low threshold suspend algorithm, sensor calibration algorithm, and Enlite sensor as the previously approved 530G pump.

The MiniMed 630G System with SmartGuard pump has some additional features compared to the MiniMed 530G System pump including:

1. A preset bolus setup allowing the user to set up a bolus to use for specific meals or snacks that are frequently consumed
2. Higher rate of insulin bolus delivery up to 15 units/minute in addition to standard 1.5 units/minute allowing for more flexibility in dosing
3. A Preset Temporary Basal allows the user to set up temporary basal rates for repeated use allowing for less button pressing when requiring a temporary basal rate
4. 8 (compared to 3) patterns for basal profile
5. An additional arrow (3 compared to 2) for high or low rate of change with sensor, providing more granular information to the user by being able to differentiate between 2 to 3 mg/dl/min and > 3 mg/dl/min. The 530G can only indicate that rates are > 2 mg/dl/min.
6. Airplane mode which temporarily stops the pump from communicating wirelessly
7. Waterproof design which protects against the effects of being underwater to a depth of up to 12 feet for up to 24 hours
8. Redesigned pump case which eliminates several known weaknesses of the 530G pump. This includes eliminating the potential for the loose drive support cap issue which was the subject of a product recall in the MiniMed 530G insulin pump
9. Color screen
10. Automatic lock feature when the pump enters sleep mode (approximately 2 minutes after entering a pre-programmed power save mode)

These additional features may contribute to benefit not only for improved usability for the user (e.g. waterproof design, color screen, etc.) but also to improve safety (e.g. elimination of known case design weaknesses as described above, automatic lock feature, etc.).

The MiniMed 630G System with SmartGuard is intended to assist patients in the management of their diabetes. The insulin infusion pump allows for continuous subcutaneous infusion of insulin at patient determined variable basal rates and intermittent patient directed bolus administration. The continuous glucose monitor provides near-continuous interstitial glucose measurement by subcutaneous sensor and tracking and trending information to supplement blood glucose measurements.

The CGM component 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 patients that they need to test their blood sugar to see if they need to take action to treat or prevent a hypoglycemic or hyperglycemic event. CGM measurements, which are performed every 5 minutes for 6 days via an indwelling sensor provide tracking and trending information to supplement the glucose meter measurements made four to seven times a day.

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 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 system screen. The system can be set to provide notifications based on sensor trends or thresholds adding information unavailable by traditional discrete monitoring. 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 settings allow for high alerts, low alerts, and Threshold Suspend alarms. With the guidance of their healthcare provider the patient can set predictive or reactive high or low thresholds to notify him or herself that the sensor glucose is approaching (the case of the predictive) or has reached (in the case of the reactive) a threshold of concern; the threshold for the Threshold Suspend feature can be similarly set to alarm and temporarily suspend insulin. 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 waken them and could proceed to severe hypoglycemia if not treated in time. Traditional blood glucose monitoring is not able to capture these potentially dangerous episodes of asymptomatic hypoglycemia. Therefore, if used as intended, this device provides significant benefit to patients not possible with traditional glucose monitoring.

The Threshold Suspend feature is an optional feature to temporarily suspend insulin delivery when the sensor glucose value reaches or goes below a preset threshold between 60 and 90 mg/dL. Hypoglycemia results because of a mismatch between the available insulin and glucose. When patients are aware of hypoglycemia by symptoms and or blood glucose check they have been instructed to treat with carbohydrates (glucose), potentially suspend the insulin pump, and repeat a blood glucose check to ensure that their blood glucose is increasing to a safer range. However, patients can have hypoglycemia unawareness and or sleep through sensor based alerts so they are unable to treat low blood glucose as instructed. Therefore, temporarily suspending insulin delivery is a limited approach to decreasing the insulin-to-carbohydrate mismatch. The currently available technology allows for the sensor to measure interstitial glucose and suspend insulin delivery when a patient set threshold has been reached. The pump will resume insulin

delivery after 2-hours have elapsed unless the patient ends the suspension earlier. Because patients with type 1 diabetes are absolutely dependent on insulin, longer suspensions increase the risk of serious hyperglycemia and ketosis.

Severe hypoglycemia can lead to seizures, unconsciousness and even death. Fear of hypoglycemia can limit the ability to adequately control hyperglycemia (which is associated with long term complications). Results from the ASPIRE study indicated that use of the Threshold Suspend feature can help to reduce the magnitude and duration of low sensor glucose events at night. Reduction in the magnitude and duration of night time low sensor glucose event in turn is likely to decrease the risk of nocturnal hypoglycemia. The greatest potential benefit of the Threshold Suspend may be for patients who have a history of hypoglycemia and who are unlikely to respond to CGM alarms and alerts at night. Potential risks of the Threshold Suspend tool include hyperglycemia, ketosis and ketoacidosis. Although not statistically powered, data from the ASPIRE in-home study suggested that using the Threshold Suspend feature may increase the risk of hyperglycemia and/or ketosis. Never-the-less, if used as intended and not as the primary method for the preventing hypoglycemia, the Threshold Suspend feature is likely to provide more benefit than risk.

Benefits of insulin therapy with continuous insulin infusion include the ability to administer insulin frequently without repeated injection; the ability to set different basal rates through the day to better match basal insulin requirements which may fluctuate during the course of the day; the ability to calculate active insulin remaining from previous boluses to avoid “insulin stacking”, which can lead to hypoglycemia; the ability to administer bolus doses over an extended time; and the ability of patient to calculate appropriate bolus insulin doses based on and their individual needs.

Risks of the CGM and Sensor include the following:

- 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.
- Prolonged insulin suspension could potentially progress to hyperglycemic crisis including diabetic ketoacidosis (DKA)
- Skin irritation, inflammation, or infection due to either the sensor needle or the adhesive
- Sensor may break leaving a sensor fragment under the skin

Risks of the Threshold Suspend feature include the following:

- The Threshold Suspend may inappropriately suspend insulin when blood glucose is above the sensor suspend threshold
- The Threshold Suspend may not appropriately suspend insulin when the blood glucose is at or below the sensor threshold suspend level
- Hyperglycemia and ketosis from automatic insulin suspension.

- Inappropriate reliance on the Threshold Suspend can result in the loss of the chance to appropriately treat hypoglycemia that can increase the risk for serious harm, seizure, and death.

Risks of the pump hardware problems include the following:

- Hypoglycemia from over-delivery of insulin 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 low-glucose alert system:

- The change in the low-glucose alert algorithm in the 630G system can miss true hypoglycemic events 0.7-4.6% more frequently compared to the 530G system. An undetected low-glucose alert can miss an opportunity to prevent severe hypoglycemia.
- The MiniMed 630G System with SmartGuard is similar to the approved MiniMed 530G System with the exception of a new hardware insulin pump platform and lower overall false alerts (modified predictive low alert algorithm). The MiniMed 630G System with SmartGuard utilizes the same low threshold suspend algorithm, sensor calibration algorithm, and Enlite sensor as the previously approved 530G pump.
- The predictive low-glucose alert algorithm is different in the 630G system compared to the 530G system. The Enlite Pivotal Study clinical dataset was used to validate the predictive low-glucose alert performance (using the 630G low-glucose alert algorithm). According to the analysis, the overall false alert rate is lower by 3.4-6.3% (across alert settings at 60, 70, 80, and 90 mg/dL) compared to the 530G system. However, the low-glucose alert system in the 630G system can miss true positive hypoglycemic alerts 0.7 to 4.6% more frequently using the same CGM alert settings compared to the 530G system. Although the "false negative" alarms appear to perform worse, the benefit such as alarm fatigue from the apparent improved false alert rate can balance the benefit compared to the risk of this feature of the 630G system.

Results from the ASPIRE study suggested that there were increased risks of hyperglycemia and potential DKA in subjects using the Threshold Suspend feature.

- Both blood ketones and urine ketones were more common in patients using Threshold Suspend. In addition,
- There was a trend towards higher glucose level in patients using Threshold Suspend (Hyperglycemia AUC with sensor glucose value > 180 mg/dL).

Though not definitive, these findings raise concern that there could be an increased risk for complications of hyperglycemia with use of the Threshold Suspend feature. This might be further amplified in patients with worse baseline control than the mean for the study population.

These additional risks for hyperglycemia and DKA identified above are described in the MiniMed 630G System with SmartGuard labelling. The risks are reasonably transparent to the patient and their physician given that they are adequately described in the labeling.

Patient Perspectives

Patient perspectives considered during the review included patient tolerance for false alerts from the predictive alert function. Reported rates of utilization of the predictive alert feature in the MiniMed 530G system have been low, and the primary reason reported by patients for not using this feature has been the high rate of false alerts. The lower false alert rate demonstrated by the predictive alert feature in the MiniMed 630G System with SmartGuard may result in increased utilization of the predictive alert feature.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks of this device for the proposed intended use.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The benefits of using the MiniMed 630G System with SmartGuard, as discussed above, outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on August 10, 2016. The final conditions of approval are cited in the approval order.

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

XIV. 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.