SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Artificial Pancreas Device System, Threshold Suspend

Device Trade Name: MiniMed 530G System

Device Procode: OZO

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

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P120010

Date of FDA Notice of Approval: September 26, 2013

Expedited: Expedited by policy[1]

II. INDICATIONS FOR USE

MiniMed 530G System

The MiniMed 530G 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 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 530G System can be programmed to automatically suspend delivery of insulin when the sensor glucose value falls below a predefined threshold value.

The MiniMed 530G System consists of the following devices that can be used in combination or individually: MiniMed 530G Insulin Pump, Enlite™ Sensor, Enlite™ Serter, the MiniLink Real-Time System, the Bayer Contour NextLink glucose meter, CareLink® Professional Therapy Management Software for Diabetes, and CareLink® Personal Therapy Management Software for Diabetes. The system requires a prescription.

[1] The Office of In Vitro Diagnostics and Radiological Health has determined that all devices intended to non-invasively monitor blood glucose, and similar devices, will be treated as expedited submissions per the Food and Drug Administration Modernization Act (FDAMA) of 1997 Section 215(b).

The MiniMed 530G System 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 530G System.

The MiniMed 530G System 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 to take measures to prevent or treat hypoglycemia himself. Therapy to prevent or treat hypoglycemia should be administered according to the recommendations of the user's Health Care Provider.

Enlite® Sensor
The Enlite Sensor is intended for use with Medtronic MiniMed 530G Insulin pump (models MMT-551, MMT-751) to continuously monitor glucose levels in persons with diabetes.

Enlite® Serter
The Enlite 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.

CareLink® Pro
CareLink Pro is designed to enhance Health Care Provider management of diabetic patients using Medtronic insulin pumps and glucose monitors and is intended for use as a tool to help manage diabetes. The purpose of this system is to take information transmitted from insulin pumps, glucose meters and continuous glucose monitoring systems, and turn it into CareLink Pro reports. The reports provide information that can be used to identify trends and track daily activities—such as carbohydrates consumed, meal times, insulin delivery and glucose readings.

CareLink® Personal
CareLink Personal is intended for use within the home and Health Care Provider environments. CareLink Personal is intended for use as a tool to help control diabetes. The purpose of this system is to take information transmitted from insulin pumps, continuous glucose monitors and glucose meters, and logbook data entered by the patient, and turn it into CareLink Personal reports.

MiniLink Real-Time System
The MiniLink Real Time System consists of the MiniLink Transmitter, a tester and a charger. When connected to a sensor that is inserted in the body, the transmitter automatically initializes the sensor and begins to periodically send glucose data to the pump using a radio signal.

III. 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.

- Do not use the Enlite Serter on products other than the Enlite sensor. Medtronic cannot guarantee this product's safety or efficacy if used on other products.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the MiniMed 530G labeling.

V. DEVICE DESCRIPTION

The MiniMed 530G System is comprised of the following devices:

MiniMed 530G Insulin Pump

The MiniMed 530G 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 infusion set.

The MiniMed 530G Insulin Pump is offered in two models (MMT-551 and MMT-751). The difference between models MMT-551 and MMT-751 is the size of the device housing to accommodate different reservoir sizes. Model MMT-551 is compatible with a 1.8 ml reservoir and model MMT-751 can be used with either the 1.8mL or the 3.0 ml reservoir. Other than the size difference in the pump case housing all other aspects of the device (PCBA, drive motor, LCD, etc.) are the same between the two models.

The MiniMed 530G Insulin Pump is similar to the Paradigm REAL-Time REVEL pump (P980022/S031, S089) hardware and software platform. The only hardware difference between the two devices is an update to the keypad overlay to include the color green to the circle around the ACT button. This is a cosmetic change and it does not affect the pump performance, function or intended use.

The major difference between MiniMed 530G Insulin Pump and the Paradigm REAL-Time REVEL insulin pump is the application software. In addition to the features carried over from the Paradigm REVEL pump, the software was updated to incorporate feature enhancements to the glucose monitoring and insulin delivery features. The feature enhancements that were included in the MiniMed 530G Insulin Pump are as follows:

- 'Threshold Suspend' tool with 60-90 mg/dL threshold range
- The sensor life has changed from three days to six days (resulting in changes to the software)

- Modified sensor calibration algorithm for the Enlite Sensor
- Blood Glucose units set to mg/dL (no longer user selectable)
- Enhanced Radio Frequency (RF) communication security features

The MiniMed 530G 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 530G Insulin Pump via RF telemetry and converted into glucose concentrations based on calibration values from 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 530G 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 530G Insulin Pump.

The most significant difference between MiniMed 530G Insulin Pump and previously approved insulin pumps is the inclusion of the 'Threshold Suspend' tool. This new tool provides the patient the means to set the pump to temporarily suspend insulin delivery automatically 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 and the programmed Suspend threshold whenever the sensor glucose value is updated (every five minutes). The use of the Threshold Suspend tool is optional and the patient can turn the tool 'ON' and 'OFF'.

When the sensor glucose value is below the set threshold, an alarm and siren 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 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 alarm and siren will then re-sound, 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 530G 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 530G Insulin Pump to continuously monitor glucose levels. It is inserted into the subcutaneous tissue of the patient and connected to a transmitter device, the MiniLink Real-Time System (model MMT-7707). 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 530G 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.

CareLink Pro Software (MMT-7335 version 3.4A):

CareLink Pro software is a personal computer software application designed to enhance Health Care Provider management of diabetic patients using compatible Medtronic insulin pumps, glucose monitors, and supported third-party blood glucose meters.

It is intended for use by the Health Care Providers in a clinical environment, as a therapy management accessory to:

- Read and store device data from supported devices.
- Read and store device data from the CareLink Personal system (MMT-7333).
- Write new device data to the CareLink Personal system.
- Generate reports from the patient records for use in managing the patient's therapy.

CareLink Personal Software (MMT-7333 version 5.9A)
CareLink Personal software is a network based software system residing on a computer server platform connected to the Internet. The system is designed to download patient data from compatible Medtronic MiniMed infusion pumps, glucose monitors, and supported third-party blood glucose meters to a central database. CareLink Personal is intended for both professional and non-professional user to facilitate the review and analysis of information downloaded from compatible devices.

MiniLink Real-Time System:
The MiniLink Real-Time System consists of the MiniLink Transmitter (model MMT-7703), Charger (model MMT-7705), and Tester (model MMT-7706).

The MiniLink 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 MiniLink 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 530G System:

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
RF Communication Devices	
CareLink USB	MMT-7305
ComLink Communication Device	MMT-7304
Paradigm Remote Control/ Programmer	MMT-503

Bayer Contour NextLink glucose meter (k122370)[2]:
The Bayer CONTOUR NEXT LINK Wireless Blood Glucose Monitoring System can directly communicate with the MiniMed 530G System. 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 530G System.

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.

2 As stated in FDA's final guidance, *The Content of Investigational Device Exemption (IDE) and Premarket Approval (PMA) Applications for Artificial Pancreas Device Systems*, because the intended use of an APDS is different than the intended use of a continuous glucose monitor (CGM), FDA believes additional information will be needed for blood glucose devices (BGD) that are part of an APDS compared to the information required for a BGD that is part of a CGM. The Agency does not intend to request this information for one year following the publication of this notice for the BGD component of APDS submissions. P120010 was received for review by the Agency within one year of guidance publication. For future APDS submissions, PMAs for APDS should include complete information (e.g., manufacturing, specifications, etc.) for the BGD component of the APDS.

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. The Medtronic MiniMed 530G System is the first device of its kind to suspend insulin when a sensor detects a pre-defined glucose threshold.

VII. MARKETING HISTORY

The MiniMed 530G System has not been marketed in the United States but a similar insulin pump system containing the threshold suspend tool received a CE mark under the name, Paradigm Real Time Veo System, and was commercialized in the European Economic Community in May 2010. The device has not been withdrawn from marketing for any reason related to its safety or 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 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. There were no Serious Adverse Device Events (SADEs) or Unanticipated Adverse Device Effects (UADEs) reported during either of the clinical studies (G110131/A001 and G100028). 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, though all sensors were inspected for fracture after removal.

A minor risk of the CCM is that patients may need to perform unnecessary fingersticks to evaluate their blood glucose when the CGM gives false positive hypoglycemic and hyperglycemic readings or alerts. There is also a minor risk of skin irritation, inflammation, or infection due to either the sensor needle or the adhesive. However, CGM devices allow patients to measure the interstitial glucose at near continuous intervals to obtain a 24 hour picture of their glucose profile, especially during the night. Tracking and trending information is of value to patients and outweighs minor risks associated with fingersticks and the sensor.

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. 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 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 or pump failure resulting in cessation of all insulin delivery due to either a hardware defect or software anomaly

For information on adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

Pre-clinical testing was performed on the insulin pump models (MMT-551 and MMT-751), Enlite Sensor (MMT-7008), Enlite Serter (MMT-7510), and MiniLink Transmitter (MMT-7707).

MMT-551 and MMT-751 Insulin Pumps
Thirty MMT-551 and 30 MMT-751 pumps were subjected to following functional and environmental tests to ensure that these devices will continue to function normally even when exposed to extreme environmental conditions:

- Storage at -20°C and 55°C
- Storage at 0% and 95% relative humidity
- Storage at 7.2 psi and 15.4 psi
- Storage at 50% relative humidity
- Exposure to detergent, alcohol, Betadine and insulin
- Temperature cycling between 3°C and 40°C
- Operation at 20% and 95% relative humidity
- Operation at 10.2 psi and 15.4 psi
- Cycling between temperature of -20°C and 60°C
- IPX4 and IPX7 liquid ingress tests
- Random vibration at 6.0 g rms in three axes
- One meter drop test
- Occlusion detection sensitivity test
- Delivery volume accuracy tests
- Battery life test
- Alarm sound lever pressure test

Pump Test Description	Test Purpose
Storage Temperature 24 Hrs at -20°C 24 hrs at +55°C	These tests determine the devices ability to function normally when exposed to extreme environmental conditions.
Storage Humidity 4 hours at 0% RH 4 hours at 95%RH	
Storage Pressure 4 hours at 7.2 psia 4 hours at 15.4 psia	
Steady State Humidity 24 hours at +50°C	

Pump Test Description	Test Purpose
96 hours at +50°C & 90%RH	
Chemical/ Fluid Compatibility Mild household liquid detergent diluted with water Quaternary Alcohol solution Betadine U100 insulin	This test determines the ability of the devices to withstand the effects of physical exposure to various chemical agents such as: a mild household liquid detergent diluted with water, a Quaternary Alcohol solution, Betadine, isopropyl alcohol, and U100 insulin.
Ingress of Liquids IPX4 and IPX7	These tests determine the devices ability to withstand accidental exposure to water and ensuring devices continue to function normally when exposed to water.
Vibration Test Random Vibration profile, 6.0 g's rms, three axes	These tests determine the ability of the devices to function normally and withstand vibration in excess of what might be experienced with normal use.
Drop Test Free-fall at height of 1 meter on 3 different starting altitudes	This test determines the ability of the devices to function normally and withstand physical shock, as might be experienced when the device is dropped.
Occlusion Sensitivity Test	This test demonstrates the ability of the devices to detect occlusion and generate an alarm "No Delivery" to notify the patient.
Delivery Volume Accuracy	This test demonstrates that the pump is able to deliver accurately (within ±5% error) while delivering during an intermediate rate.
Battery Life Test	This test demonstrates that the pump is able to detect low voltage of the battery and generate a Low Battery or dead battery (Off No Power) alarm to notify the patient to replace the battery of the pump.
Six Day Sensor	This test demonstrates the ability of the devices to calculate the age of the sensor and generate “End Sensor” alarm after six days of use.
Self Coexistence Test	This test demonstrates the ability of multiple devices to continue RF communication when they are in close proximity.
Alarm Sound Level Pressure Test	This test demonstrates the ability of the devices to generate audio alarm loud enough to be heard by the patient during alarm conditions.
Ship Test	This test demonstrates the ability of the packaging to protect the devices during shipping.
Leap Year Verification	This test demonstrates the ability of the devices to function normally during date changes in leap years.

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

MMT-7008 Enlite Sensor

Sixty model MMT-7008 sensors were subjected to the following functional and environmental test after sterilization and six month aging at 30°±2°C:

- Extraction test
- Water tightness test
- Latching test
- Insertion test (pork shoulder)
- Needle hub pull test
- Electrical connection test
- Sensor pull break test
- Insertion force test
- Hot water seal integrity test
- Accuracy test
- Linearity test
- Response time test
- Sensor stability test
- Operating temperature test
- Oxygen effect test
- Ascorbic acid interference test
- Acetaminophen interference test

Sensor Test Description	**Test Purpose**
Extraction Test	To test the force required to extract the needle after insertion.
Water Tightness Test	To test the ability of the connection between the sensor and the transmitter to prevent water from entering the transmitter bore.
Latching Test	To test that the connection to the transmitter is robust.
Insertion Test (Pork Shoulder)	To test the overall mechanical functionality of the device in a representative use-case scenario.
Needle Hub Pull Test	To test the robustness of the needle hub assembly.
Electrical Connection Test	To test the resiliency of the sensor contact pads after multiple connect/disconnect cycles.
Sensor Pull Break Test	To test mechanical integrity of the sensor/tube assembly.
Insertion Force Test	To test the force required to insert the sensor.
Hot Water Seal Integrity Test	To test that there is no fluid path between the insertion site and the sensor connector that would allow body fluids to reach the transmitter.
Accuracy Test	To test that the sensor output is within the system

Sensor Test Description	Test Purpose
	required limits at the extent of the glucose ranges (40mg/dL and 400mg/dL).
Linearity Test	To test that sensors show a linear response when glucose levels are driven from 40mg/dL to 400 mg/dL in a stepwise manner.
Response Time Test	To test that the sensor responds adequately to sudden changes in glucose concentration.
Sensor Stability Test	To test that the sensor's signal remains stable throughout the wear period.
Operating Temperature Test	To test that the sensor's signal remains stable when subject to changes in external temperature during the wear period.
Oxygen Effect Test	To test the sensor's response to variation in oxygen concentration of the surrounding environment.
Ascorbic Acid Interference Test	To test the sensor's response to the introduction of ascorbic acid in the surrounding environment.
Acetaminophen Interference Test	To test the sensor's response to the introduction of acetaminophen in the surrounding environment.

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

Enlite Serter (MMT-7510)

Fifty-nine MMT-7510 Serters (60 for chemical exposure tests) were subject to the following functional and environmental test after six month aging at room temperature:

- Storage at -20°C and 55°C
- Storage at 0% and 95% relative humidity
- Storage at 7.2 psi and 15.4 psi
- Exposure to detergent, alcohol, Betadine and insulin
- Trigger release force test
- Trigger arming force test
- Sensor ejection test
- Sensor insertion test
- Insertion cycles (600 insertions) following temperature cycling
- One meter drop test

Serter Test Description	Test Purpose
Storage at -20°C and 55°C	To test that the device works with the required storage requirements.
Storage at 0% and 95% relative humidity	To test that the device works with the required humidity requirements.

Serter Test Description	Test Purpose
Storage at 7.2 psi and 15.4 psi	To test that the device works with the required atmospheric requirements.
Exposure to detergent, alcohol, insulin, disinfectant	To demonstrate that the external surfaces of the device and device are not damaged when subjected to U100 insulin or equivalent, mild household detergent or bleach.
Trigger Release Force Test	To test that the trigger force shall be no higher than 7 lbs. and that the device does not fire without depressing and releasing trigger.
Trigger Arming Force Test	To test that the Trigger force shall be no higher than 7 lbs.
Sensor Ejection Test	To test that the device can eject sensor needle hub.
Sensor Insertion Test	To test that sensor does not dislodge from device and that the device can insert the sensor assembly.
Insertion cycles following temperature cycling	To test that the device functions when subjected to extreme temperatures (-20C; 60C) and after each cycle of 600 cycles
Drop Test	To test that device maintains functionality when dropped from a height of 1 meter.

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

MiniLink Transmitter (MMT- 7707)

Thirty (30) MiniLink (MMT-7707) transmitters 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:

- Storage at -20°C and 55°C
- Storage at 0% and 100% relative humidity
- Storage at steady state 37°C & 90%RH
- Chemical/Fluid compatibility
- Liquid ingress testing
- Drop Test
- Connector Cycling Test
- Battery Life Test

Transmitter Test Description	Test Purpose
Storage Temperature 24 Hrs at -20°C 24 hrs at +55°C	A performance test designed to demonstrate that the devices can function within the established operating parameters under the specified environmental conditions for storage temperature extremes as stated in the product specification.
Storage Humidity 4 hours at 0% RH 4 hours at 100%RH	A performance test designed to demonstrate that the devices can function within the established operating parameters under the specified environmental conditions for storage humidity extremes as stated in the product specification.
Steady State Humidity 72 hours at +37°C & 90%RH	A performance test designed to demonstrate that the devices can function within the established operating parameters under the specified environmental conditions for long-term operating humidity exposure as stated in the product specification.
Chemical/ Fluid Compatibility	This test determines the ability of the devices to withstand the effects of physical exposure to various chemical agents that the device may encounter in a normal-use environment.
Ingress of Liquids IPX8: 8ft submersion for 30 minutes	A performance test designed to demonstrate the ability of the device to withstand complete water immersion for the specified depth and dwell time.
Mechanical Vibration Test	A mechanical stress test designed to demonstrate the ability of the device to withstand the specified condition of random vibration to show that the material strength exceeds the stress.
Drop Test	A mechanical stress test designed to demonstrate the ability of the device to withstand the impact resulting from a 1 meter freefall to show that the material strength exceeds the stress.
(Sensor) Connector Cycling Test	A mechanical stress test designed to demonstrate the ability of the device to withstand and function following exposure to the repeated cyclic stress of 244 sensor insertions to show that the material strength exceeds the stress.
(Charger) Connector Cycling Test	A mechanical stress test designed to demonstrate the ability of the device to withstand and function following exposure to the repeated cyclic stress of 244 charger insertions to show that the material strength exceeds the stress.
Battery Life Test Time to low battery message	A performance test designed to demonstrate the ability of the device to within the established timing parameters as stated in the product specification.

Transmitter Test Description	Test Purpose
Battery Life Test Low battery message sustain period	

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

Electromagnetic Compatibility Testing: The MMT-551 and MMT-751 insulin pumps were subjected to the following tests to confirm that electromagnetic emissions for these devices were within acceptable limits and that these devices will continue to function properly in the presence of electromagnetic signals that may be encountered in the intended use environment:

- ESD exposure (indirect discharge)
- ESD exposure (direct discharge)
- Radiated emissions
- Radio frequency field immunity
- Power frequency magnetic field immunity
- Commercial avionics immunity
- Electronic article surveillance equipment immunity
- Cell phone immunity
- Metal detector immunity
- Household emitters immunity
- X-ray immunity
- DC magnetic field/MRI immunity
- Wireless coexistent/immunity

EMC Test Description	Test Purpose
Electrostatic Discharge Immunity ESD Indirect Discharge ESD Direct Air Discharge	These tests demonstrate the ability of the pumps to either operate properly in an environment with high level of electrostatic discharge (ESD) or to cease its operation and assert an alarm when erroneous signals are detected.
Electro-Magnetic Emission Radiated RF Emission FCC part 15 Subpart C section 15.249 (a)	These tests demonstrate the ability of the pumps to either operate properly in an environment with high level of electromagnetic emission or to cease its operation and assert an alarm when erroneous signals are detected.

EMC Test Description	Test Purpose
Radio Frequency Field Immunity	The immunity tests demonstrate that the device will operate within its specification when exposed to electromagnetic interference at the levels in excess of those expected in normal use environment.
Power Frequency Magnetic Field Immunity	
Commercial Avionics Immunity	
Electronic Article Surveillance Immunity	The immunity tests will demonstrate that the device will operate within its specification when exposed to electromagnetic interference at the levels in the excess of those expected in normal use environment.
Cell Phone Immunity	
Metal Detector Immunity	
Household Emitter Immunity	
X-ray Immunity	
DC Magnetic Field Immunity	
Wireless Coexistence Immunity	

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

Biocompatibility: The sponsor referenced biocompatibility testing in previously approved submissions for the materials that comprise the MiniMed 530G Insulin Pump, the MiniLink transmitter, the insulin reservoirs and the insulin infusion sets to support approval of the 530G System. This was evaluated and approved as part of previous submissions to the FDA and was not repeated for this submission. Biocompatibility testing for the sensor components (Patch, tube and circuits) was performed in accordance with the recommendations of ISO1 10993-1 Annex A. The results of these tests are listed in Table 1 -3 below.

Table 1: Adhesive Patch Biocompatibility Tests

Test	ISO Standard	Result
Cytotoxicity	ISO 10993-5	Pass – non-cytotoxic
Sensitization (closed patch	ISO 10993-10	Pass – no evidence of

Test	ISO Standard	Result
method)		sensitization
Irritation (intracutaneous reactivity)	ISO 10993-10	Pass – negligible irritation response

Table 2: Sensor Tube Biocompatibility Tests

Test	ISO Standard	Result
Cytotoxicity	ISO 10993-5	Pass – non-cytotoxic
Sensitization (delayed hypersensitivity)	ISO 10993-10	Pass – no evidence of sensitization
Irritation (intracutaneous reactivity)	ISO 10993-10	Pass – negligible irritation response
Systemic Toxicity (acute)	ISO 10993-11	Pass – non-toxic
Sub-chronic (sub-acute) Toxicity	ISO 10993-11	Pass – non-toxic
Genotoxicity	ISO 10993-3	Pass – non-genotoxic
Implantation	ISO 10993-6	Pass – non-irritating

Table 3: Sensor Circuit Biocompatibility Tests

Test	ISO Standard	Result
Cytotoxicity	ISO 10993-5	Pass – non-cytotoxic
Sensitization (delayed hypersensitivity)	ISO 10993-10	Pass – no evidence of sensitization
Irritation (intracutaneous reactivity)	ISO 10993-10	Pass – negligible irritation response
Systemic Toxicity (acute)	ISO 10993-11	Pass – non-toxic
Sub-chronic (sub-acute) Toxicity	ISO 10993-11	Pass – non-toxic
Genotoxicity	ISO 10993-3	Pass – non-genotoxic
Implantation	ISO 10993-6	Pass -
Hemolysis	ISO 10993-4	Pass – non-hemolytic
Material Mediated Pyrogenicity	ISO 10993-11	Pass – non-pyrogenic

Sterility: The electron beam sterilization process was used to sterilize the MMT-7008 (Enlite) sensor according to the requirements of EN ISO 11137. The Enlite sensor is a single use disposable device that is provided sterile and is intended to be worn for up to 6 days. The minimum dose based on the device bioburden is 16.7 kGy for a SAL of 10-6. Sterilized components meet EN ISO 11137 Sterilization of Health Care Products – Radiation and the process was validated according to EN ISO 11137. Results demonstrate that the electron beam sterilization process for the Enlite Sensor consistently achieve a SAL of 10-6 for adequate sterilization.

The sponsor referenced sterility testing in their previously approved submissions for the materials that comprise the MiniMed 530G Insulin Pump, the MiniLink transmitter, the insulin reservoirs and the insulin infusion sets to support approval of the 530G

System. The Sterilization processes for the other sterile accessory components of the system (insulin pump reservoirs and tubing sets) were reviewed under previous applications to the FDA and were not repeated in this submission. The remaining system components (MiniMed 530G insulin pump, etc.) are provided non-sterile.

Packaging/Shelf-Life: The packaging of the Enlite Sensor (MMT-7008) was validated for a shelf life of six months according to the requirements of ISO 11607, ASTM D 4169 and ASTM F 1929-98. The Enlite Sensor has a 6-month shelf life when stored at +2ºC to +30ºC. The Enlite Sensors are packaged individually in clear, plastic rigid trays (glyco-modified polyethylene terephthalate) with heat sealed Tyvek lids. The sensors are packed in a customer box, which contains 1 or 5 units and over-tape. The box with 1 unit is identified as MMT-7008B the box with 5 units is identified as MMT-7008A. After packaging, the sensors are sterilized. Results demonstrated that the Enlite Sensor is adequately packaged for sterilization and protection of the device.

The Enlite Serter is a skin contacting device that is not sterile. It is packaged and shipped in a cardboard box with partitions. The Enlite Serter is placed into the cavity formed by the partitions. The instructions for use sheets are placed on top of the Serter and the lid is closed and secured with a label seal. Final packaging configuration was qualified to meet the standards ASTM D4169 and ASTM D642-00 Standard Test Method for Determining Compressive Resistance of Shipping Containers, Components, and Unit Loads. The purpose of the testing was to evaluate the stand-alone packaging of the product box and interior partitioning potentially to be used in the shipment of new product finished goods inventory. Results demonstrated that the Enlite Serter is adequately packaged for protection of the device during shipping and distribution.

The sponsor referenced packaging testing in their previously approved submissions for the materials that comprise the MiniMed 530G Insulin Pump, the MiniLink transmitter, the insulin reservoirs and the insulin infusion sets to support approval of the 530G System. Therefore, packaging for the remaining components of the MiniMed 530G system were validated as part of previously reviewed submissions to the FDA and were not repeated in this submission.

Shipping Testing: Shipping distribution testing for the Enlite Sensor was conducted per ASTM D4169-09 with environmental conditioning under winter and summer conditions, instead of the ambient conditions described in the standard. This deviation from the standard was determined to be acceptable. For Summer conditions, the temperature and humidity were cycled between 30°C/40% RH to 50°C/85% over 13 periods, with 2 hr periods at 50°C/85% RH and 1-3 days at 30°C/40% RH. For Winter conditions, the temperature was cycled between -20°C and 10°C over 13 periods with 2 hr periods at -20°C and 1-3 days at 10°C.

The firm conducted environmental conditioning and simulated shipping hazard exposure following Distribution Cycle (DC) 13 at Assurance Level I: Climate Conditioning, Manual Handling (Sequence 1 and 2), Vehicle Stacking, Vehicle

Vibration, Loose Load Vibration, and Concentrated Impact testing. Schedule I low pressure vacuum testing (per DC 13) is not required and thus was not conducted because the packaging is breathable. Three shippers were tested and included fully functional and dummy sensors. Results demonstrated that package integrity for the Enlite Sensor is maintained following shipping and distribution.

As stated above in the "Packaging/Shelf-Life" section, final packaging configuration for the Enlite Serter was qualified to meet the standards ASTM D4169 and ASTM D642-00 Standard Test Method for Determining Compressive Resistance of Shipping Containers, Components, and Unit Loads. Results demonstrated that the Enlite Serter is adequately packaged for protection of the device during shipping and distribution.

Software: Comprehensive testing was performed to confirm that the threshold suspend tool software associated with the MiniMed 530G system and the CareLink Pro software and CareLink Personal software) meets all specified requirements and that these software will operate reliably and safely under normal or abnormal use conditions.

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 requirement, 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/Usability: Initial usability testing (user-interface design validation) of the MiniMed 530G System was performed. The testing considered device users, use environment, and user interfaces including device labeling and training. Additional usability testing will also be conducted with the MiniMed 530G System during a post approval study with a final version of the device labeling. Testing during the post approval study will further assess the adequacy of the labeled user instructions and training materials to support safe and effective use and will emphasize the usability of the threshold suspend tool.

B. Animal Studies

None

C. Additional Studies

None

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed two pivotal clinical studies to establish a reasonable assurance of safety and effectiveness of the MiniMed 530G System for its intended use. These studies were performed in the United States under IDE # G110131/A001 and G100028.

Data from these clinical studies were the basis for the PMA approval decision. A summary of each of these clinical studies is presented below.

CLINICAL STUDY	IDE Number	PATIENT POPULATION	STUDY DESIGN
A Performance Evaluation of the Enlite™ Glucose Sensor to Support a Full 144 Hours (6 Days) of Use	G110131/A001	Adult (Age 18-75)	A multi-center, randomized, prospective correlational study, designed to determine the Enlite sensor accuracy when minimally calibrated
An In-clinic, Randomized, Cross-Over Study to Assess the Efficacy of the Threshold Suspend Feature in the MiniMed Paradigm® X54 System with Hypoglycemic Induction from Exercise	G100028	Adult/Young Adult (Age 17-60)	A randomized, crossover study with a run-in period of the use of the Sof-Sensor and the MiniMed Paradigm® X54 System (with the Threshold Suspend tool), designed to assess the efficacy of the Threshold Suspend tool in reducing hypoglycemia.

A. Study Design

G110131/A001 - Performance Evaluation of the Enlite™ Glucose Sensor

This was a multi-center, randomized, prospective correlational study, designed to determine the accuracy of the Enlite sensor in adults with type I or type II diabetes between the ages of 18 – 75. Sensor accuracy was determined by comparing calibrated glucose sensor values to reference plasma glucose values during the in-clinic 12 hour monitoring portions of the study. In-clinic testing consisted of frequent sample testing (FST) of blood samples obtained every 5-15 minutes on Day 1, Day 3, and Day 6 of the study.

Subjects previously diagnosed with type I or type II diabetes were enrolled at seven investigational sites. Subjects received two Enlite sensors placed as follows using a 1:1:1 randomization scheme: both placed on the abdomen; both placed on the buttocks; or one placed on the abdomen and one placed on the buttock. Each sensor was associated with its own transmitter (MiniLink) and MMT-x23S insulin pump. The insulin pump was only used as a display for the Enlite sensor and was not delivering insulin during the study.

Subjects were instructed to calibrate one of the two sensors 3-4 times over the course of the FST visit days and the other sensor according to the minimum calibration requirements (every 12 hours after the second calibration). During home use (outside

the clinic), subjects were instructed to calibrate both sensors 3-4 times a day. During each FST visit, subjects underwent a hypoglycemic challenge (glucose lowered to a target of 50-75 mg/dL for ~2 hours, including 30 minutes between 50-60 mg/dL) and a hyperglycemic challenge (glucose raised to a target of 180-400 mg/dL for ~2 hours, including 30 minutes between 350 -400 mg/dL). In-clinic blood glucose levels were determined using a reference method (YSI) and were compared to sensor readings. Subjects were monitored carefully through all hypoglycemic and hyperglycemic challenges. Safety procedure guidelines were established and followed for all challenges.

Glucose sensor values obtained outside the clinic were compared to values obtained through self-monitoring of blood glucose (SMBG) using the patient's preferred glucose meter.

1. Clinical Inclusion and Exclusion Criteria
   Enrollment in the G110131/A001 study was limited to patients who met the following *inclusion criteria*:

   a) Subject is 18 - 75 years of age at time of screening
   b) A clinical diagnosis of type 1 or 2 diabetes as determined by the Investigator, for a minimum of 12 months duration:
      Criteria for *type 1* diabetes:
      - Required: Age of onset < 40 years of age
      - Required: History of insulin use only for management of diabetes
      - Required: History of normal weight or underweight at time of diagnosis.
      - Not required: Initial presentation of diabetic ketoacidosis.
      - Not required: History of diabetic ketoacidosis (DKA)
      - Not required: Low fasting C-peptide
      - Not required: Autoantibodies (i.e. GAD or ICA)

      Criteria for *type 2* diabetes:
      - Required: Age of onset > 40 years of age
      - Required: History of initial oral anti-diabetic use
      - Required: History of being at least overweight at time of diagnosis.
      - • Type 2 insulin requiring is defined by type 2 diabetes subjects taking insulin with or without oral anti-diabetic agent and may also include: incretin mimetic, pramlintide or GLP agonist
        • Type 2 non-insulin requiring is defined by type 2 diabetes subjects who take oral medications and may also include: incretin mimetic, pramlintide, or GLP agonist
   c) Adequate venous access as assessed by investigator or appropriate staff

   Patients were not permitted to enroll in the G110131/A001 study if they met any of the following *exclusion criteria*:
   a) Subject is unable to tolerate tape adhesive in the area of sensor placement.
   b) Subject has any unresolved adverse skin condition in the area of sensor or device placement (e.g., psoriasis, rash, *Staphylococcus* infection)

c) Subject is actively participating in an investigational study (drug or device) wherein they have received treatment from an investigational drug or device in the last 2 weeks
d) Subject has a positive pregnancy screening test
e) Subject is female and plans to become pregnant during the course of the study
f) Subject has had a hypoglycemic seizure within the past 6 months
g) Subject has had hypoglycemia resulting in loss of consciousness within the past 6 months prior to screening visit.
h) Subject has had an episode of DKA within the past 6 months prior to screening visit.
i) Subject has a history of a seizure disorder
j) Subject has central nervous system or cardiac disorder resulting in syncope
k) Subject has a history of myocardial infarction, unstable angina, coronary artery bypass surgery, coronary artery stenting, transient ischemic attack (TIA), cerebrovascular accident (CVA), angina, congestive heart failure, ventricular rhythm disturbances or thromboembolic disease
l) Subjects with hematocrit lower than the normal reference range
m) Subjects with a history of any cardiac arrhythmia, including atrial arrhythmias
n) Subjects with a history of adrenal insufficiency
o) Subjects with history of migraines that have occurred at least 2 times in the last 3 months prior to enrollment.

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 irritations) and evaluated safety issues related to system use during the study. No long-term follow up was included in this study protocol.

G100028 - Study to Assess the Efficacy of the Threshold Suspend Feature in the MiniMed Paradigm® X54 System

This was a multi-center, in-clinic, randomized, cross-over study with run in period, designed to assess the efficacy of the Threshold Suspend tool in reducing exercise induced hypoglycemia in subjects with type I diabetes. The study was performed with the Veo MMT-X54 insulin pump and the Sof-Sensor (MMT-7003) glucose sensor. The Veo insulin pump utilizes the same calibration algorithm and threshold suspend software used in the MiniMed 530G system.

The primary treatment comparison was the duration (min) and severity (lowest mg/dL) of induced hypoglycemia.

Fifty (50) subjects previously diagnosed with type I diabetes on current insulin pump therapy were enrolled at five sites.

There were twelve (12) study visits. Prior to randomization, each subject was required to perform a 2-week run-in period (Visits 1 – 6). They included: screening (Visit 1), enrollment (Visit 2), 3 phone visits (to verify that the subject's basal rates

were appropriate and to make any adjustments, if needed (Visits 3-5)), and an exercise run-in visit (Visit 6). During Visit 6, a safe rate of decline in glucose level was determined for each subject. Following the run-in period, subjects were randomized into 2 groups (Visit 7):

- Group A:
  - Period 1: subjects wore the Medtronic MiniMed Paradigm® X54 System with the threshold suspend tool turned '**ON**' during the exercise induced hypoglycemia visit.

- Group B:
  - Period 1: subjects wore the Medtronic MiniMed Paradigm® X54 System with the threshold suspend tool turned '**OFF**' during the exercise induced hypoglycemia visit.

Subjects crossed over (turned threshold suspend tool on /off) after Visit 9.

- Group A:
  - Period 2: subjects wore the Medtronic MiniMed Paradigm® X54 System with the threshold suspend tool turned '**OFF**' during the exercise induced hypoglycemia visit.

- Group B:
  - Period 2: subjects wore the Medtronic MiniMed Paradigm® X54 System with the threshold suspend tool turned '**ON**' during the exercise induced hypoglycemia visit.

1. <u>Clinical Inclusion and Exclusion Criteria</u>
   Enrollment in the G100028 study was limited to patients who met the following *inclusion criteria*:
   a) Subject is between the ages of 16 - 60 years old;
   b) Subject must weigh > 45 kg at the time of enrollment;
   c) A clinical diagnosis of Type 1 Diabetes Mellitus, as determined by the Investigator, for a minimum of 12 months duration;
   d) Subject has been on a Medtronic insulin pump for at least three (3) months, which includes but is not limited to those on sensor augmented insulin pump therapy;
   e) Subject has a HbA1c value between approximately 7.0% and 10.0% at time of enrollment; as measured during the screening visit;
   f) Subject is able to exercise as determined by the Investigator for an extended period of time, according to study requirements;
   g) Subject must have a documented stress treadmill test within the last three years of enrollment if the subject had diabetes for 20 years;
   h) If subject has celiac disease, it has been adequately treated as per investigator discretion;
   i) Subject is willing to follow protocol and procedures for study.

Patients were not permitted to enroll in the G100028 study if they met any of the following *exclusion criteria*:

a) Systolic blood pressure on screening visit is ~ 140 mmHg;
b) Diastolic blood pressure on screening visit is ~ 90 mmHg;
c) Subject has a history of hypoglycemic seizure or hypoglycemic coma within the last two years;
d) Subject unable to tolerate tape adhesive in the area of sensor placement;
e) Subject has any active adverse skin condition in the area of sensor placement (i.e. psoriasis, rash, staphylococcus infection) that is not resolved at the time of enrollment;
f) Subject is pregnant or plans to become pregnant during the course of the study;
g) Subject has a history of myocardial infarction, unstable angina, coronary artery bypass surgery, coronary artery stenting, transient ischemic attack (TIA), cerebrovascular accident (CVA), angina, congestive heart failure, ventricular rhythm disturbances or thromboembolic disease;
h) Subject has active Graves disease;
i) Subject with renal impairment or Creatinine above the normal reference range (of the laboratory that the clinical site is utilizing), as demonstrated by the screening laboratory value;
j) Subject is outside of the normal reference range (of the laboratory that the clinical site is utilizing) for Hematocrit, as demonstrated by screening laboratory value;
k) Subject is outside of the normal reference range (of the laboratory that the clinical site is utilizing) for Potassium, as demonstrated by screening laboratory value;
l) Subject is outside of the normal reference range (of the laboratory that the clinical site is utilizing) for TSH, as demonstrated by screening laboratory value;
m) Subject is outside of the normal reference range (of the laboratory that the clinical site is utilizing) for free T4, as demonstrated by screening laboratory value;
n) Subject has history of smoking for ~ 5 years;
o) Electrocardiogram (ECG / EKG) findings observed during the screening visit, which are deemed by the investigator to represent active ischemia or a condition that would compromise subject safety;
p) The stress treadmill (if subject met inclusion criteria #7) results are deemed by the investigator to represent active ischemia or a condition that would compromise subject safety;
q) Subject is currently participating in an investigational study (drug or device);
r) Subject is currently on beta blocker medication;
s) Subject has taken oral or injectable steroids within the last 30 days;
t) Subject is deemed by the Investigator to be unwilling or unable to follow the protocol;
u) Subject has a history of diagnosed medical eating disorder;
v) Subject has a history of known illicit drug abuse;
w) Subject has a history of known abuse with prescription medication;

x) Subject has a history of visual impairment which would not allow subject to participate in the study and perform all study procedures safely per investigator discretion;
y) Subject has a history of current alcohol abuse;
z) Any other condition including abnormalities found on the screening tests which in the opinion of the Investigator, may preclude him/her from participating in the study.

2. Follow-up Schedule

At the end of study, subjects removed all study devices. Study investigators documented any Adverse Device Effects (including 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

The duration (min) and severity (mg/dL) of induced hypoglycemia was evaluated.

The secondary endpoints were the evaluation of:

- Hypoglycemia Area under the Curve (AUC) (YSI blood glucose < 60 mg/dL)
- Hypoglycemia AUC (YSI blood glucose < 70 mg/dL)
- Hyperglycemia AUC (YSI blood glucose>180 mg/dL)
- Accuracy of the sensor glucose values measured against the YSI glucose values at levels <90 mg/dL.
- Last YSI blood glucose reading, four (4) hours after subject has reached target range of <70 mg/dL by YSI
- Number of times the study was terminated for low (50 mg/dL YSI) or high (300 mg/dL YSI) blood glucose.
- Incidence of true positive, false positive or false negative activation of the LGS tool.

B. Accountability of PMA Cohort

G110131/A001

Of the 90 subjects that entered the study, all but one subject participated in all in-clinic and the home portions of the study. Ninety subjects participated in the first FST visit (with 90 subjects having 12 hours of frequent sampling data), 90 subjects participated in the second FST visit (with 90 subjects having 12 hours of frequent sampling data), and 89 subjects participated in the third FST visit (with 89 subjects having 12 hours of FST data).

G100028

Of the 50 subjects that entered the study, all but two subjects participated in all in-clinic induction experiments of the study. A total of 134 experiments were performed. Of the 134 hypoglycemic induction experiments performed, 98 hypoglycemic induction experiments were successful. A successful induction was

defined as having an observation period of 3-4 hours without needing safety intervention. Thirty-six hypoglycemic induction experiments were determined to be unsuccessful either because of failure induce hypoglycemia (YSI < 70 mg/dL) or to prevent severe hypoglycemia (YSI < 50 mg/dL), and required the subject to repeat the induction visit.

C. Study Population Demographics and Baseline Parameters

G110131/A001

A total of 90 subjects were successfully screened and enrolled in the study. The average age at time of randomization was 44.4 years old (SD 13.8, range, 18 – 71). Forty six percent (n = 41) of subjects were female. Subjects predominantly self-identified as Caucasian (87.8%).

Twenty eight percent (n = 25) of subjects were diagnosed with type II diabetes; 72% (n = 65) were diagnosed with type I diabetes.

The mean body mass index (BMI) was 28.8 (SD 7.4, range 16.9 - 50.7). Two percent (n = 2) of subjects were underweight; 31.1% (n = 28) were normal weight; 58.9% (n = 53) were overweight or obese; 7.8% (n = 7) were morbidly obese.

Thirty eight percent of subjects (n = 34) did not have any prior experience using a continuous glucose monitoring system.

G100028

Fifty (50) subjects (17-58 years old) were randomized and completed the study. The study included two (2) age cohorts. Forty-two (42) subjects enrolled in the adult (≥ 22 years) cohort;(mean 37.4, SD 11.0). Eight (eight) subjects were enrolled in the pediatric (≤ 21years) adolescent cohort; four (4) subjects ages 18-20 years (mean 19.25, SD 0.96) and four (4) subjects age 17.

Subjects in the pediatric adolescent cohort were predominantly male (7/8, 87.5%). 50% of the adult subjects were female. Ninety-six percent (96%, 48/50) of enrolled subjects self-identified as Caucasian.

The mean body mass index (BMI) was 25.7 (SD, 3.4), 24.3 (SD, 3.4), and 27.3 (SD, 4.4) in the 16-17 year old, 19-21 year old, and adult cohorts, respectively.

D. Safety and Effectiveness Results

G110131/A001

1. Safety Results

   The analysis of safety was based on the 90 subjects that participated in the study. Investigators were instructed to monitor the subjects throughout the course of the study for the occurrence of an adverse event. During the frequent sampling

hypoglycemic and hyperglycemic challenges investigators (medical physicians) were available at all times. There were no symptoms of nausea, vomiting, or abdominal pain associated with the FST visits. The symptoms described included:

- Hunger or discomfort (i.e., "patient uncomfortable or not feeling well")
- Adrenergic and neuroglycopenic symptoms of hypoglycemia, which included shakiness, diaphoresis, weakness, jittery feeling, tingling
- Pain or discomfort related to the IV
- Headache and fatigue

The safety data of the Enlite Sensor were assessed by evaluation of the incidence of all Adverse Device Effects (ADEs), Serious Adverse Device Events (SADEs), and Unanticipated Adverse Device Effects (UADEs) experienced by study subjects. Adverse events (AEs) were listed in terms of severity and relationship to 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.

Adverse effects that occurred in G110131/A001:

Twenty-two adverse events were reported to the sponsor, with 21 events categorized as being mild intensity and 1 adverse event categorized as moderate intensity (not related to device or study procedure). All adverse events were resolved and subjects recovered completely without sequelae.

- There was one moderate-intensity adverse event of sinusitis that was not related to the study devices or procedures.
- There was one adverse event that was device related which was mild in intensity. At the sensor removal visit the subject reported pain at sensor insertion site during sensor wear.
- There were 7 procedure-related adverse events all of which were mild in intensity. Five participants reported pain and discomfort related to the IV catheter. One event was a headache occurring at the beginning of the hyperglycemic challenge. One subject noted edema in their left hand related to heating pad placement.
- There was one report of chest pain described as mild pressure in mid-chest, recorded as a mild adverse event not related to the device or study procedure. Vitals, electrocardiogram, and physical exam were determined to be normal by the physician investigator. Physician investigator believed it could be musculoskeletal or gastroesophageal reflux disease. Symptoms resolved four hours later.
- There was one report of hypoglycemia that occurred during out of clinic period – the subject awoke with blood glucose value of 49 mg/dL. The subject did not require assistance and recovered after ingesting carbohydrates.
- The other 11 adverse events were not related to study device or procedure and primarily consisted of upper respiratory infections; sinusitis; flu; cold and bowel symptoms.

There were no reports of serious adverse events or unanticipated adverse device effects during the study.

2. Effectiveness Results

Key effectiveness outcomes are presented in tables 1 to 33.
(Note – Although data was collected for Enlite sensors (MMT-7008) inserted in both the abdomen and buttock during the study, since the recommended insertion site for the Enlite sensor will be limited to the abdomen, the effectiveness results discussed in the following section are limited to abdominal sensors.)

Table 1. CGM difference to YSI within YSI glucose ranges; Calibrating three to four times daily, Abdomen insertion site.

YSI glucose ranges (mg/dL)	Number of paired CGM-YSI	Mean percent difference (%)	Median percent difference (%)	Mean absolute percent difference (%)	Median absolute percent difference (%)
Overall	7415	2.05	0.93	13.63	10.10
<40*	3	28.18	31.65	28.18	31.65
40-60*	618	6.50	5.45	10.06	7.85
61-80*	1419	4.81	3.80	11.43	9.05
81-180	3241	1.95	1.72	12.38	9.09
181-300	1648	-2.79	-2.47	11.72	8.96
301-350	325	-6.32	-5.36	11.36	8.43
351-400	137	-11.99	-9.23	13.48	10.11
>400	24	-28.38	-26.78	28.38	26.78

***** *For YSI reference range ≤ 80 mg/dL, the differences are reported in mg/dL instead of percent difference (%).* ***Note:*** *CGM Readings are within 40-400 mg/dL.*

Table 2. CGM difference to YSI within YSI glucose ranges; Calibrating every 12 hours, Abdomen insertion site.

YSI glucose ranges (mg/dL)	Number of paired CGM-YSI	Mean percent difference (%)	Median percent difference (%)	Mean absolute percent difference (%)	Median absolute percent difference (%)
Overall	7432	0.75	0.74	14.71	10.80
<40*	3	27.18	27.65	27.18	27.65
40-60*	515	6.56	4.75	11.07	9.15
61-80*	1349	1.36	-0.15	12.04	9.90
81-180	3158	2.14	3.00	13.95	10.45
181-300	1895	-3.02	-1.03	12.62	8.54
301-350	346	-6.50	-2.08	12.27	6.97
351-400	132	-12.06	-7.98	13.68	8.29
>400	34	-28.08	-19.87	28.08	19.87

***** *For YSI reference range ≤ 80 mg/dL, the differences are reported in mg/dL instead of percent difference (%).* ***Note:*** *CGM Readings are within 40-400 mg/dL.*

Table 3. CGM difference to YSI within CGM glucose ranges; Calibrating three to four times a day, Abdomen insertion site.

CGM glucose ranges (mg/dL)	Number of paired CGM-YSI	Mean percent difference (%)	Median percent difference (%)	Mean absolute percent difference (%)	Median absolute percent difference (%)
Overall	7415	1.61	-0.93	13.99	10.00
40-60*	620	9.07	6.30	10.38	7.25
61-80*	1240	-0.86	-3.67	10.37	8.05
81-180	3497	-0.02	-2.03	13.96	9.82
181-300	1675	1.99	0.68	12.29	9.17
301-350	266	-1.71	-1.50	9.47	6.89
351-400	117	-6.68	-6.66	9.31	7.77

For CGM range ≤ 80 mg/dL, the differences are reported in mg/dL instead of percent difference (%).

Table 4. CGM difference to YSI within CGM glucose ranges; Calibrating every 12 hours, Abdomen insertion site.

CGM glucose ranges (mg/dL)	Number of paired CGM-YSI	Mean percent difference (%)	Median percent difference (%)	Mean absolute percent difference (%)	Median absolute percent difference (%)
Overall	7432	4.42	-0.73	16.69	10.56
40-60*	755	15.88	10.70	17.24	11.05
61-80*	975	1.85	-0.90	10.99	7.50
81-180	3423	2.08	-2.80	16.95	11.40
181-300	1810	0.16	-1.34	11.32	7.69
301-350	342	-2.57	-1.57	8.35	6.20
351-400	127	-6.00	-6.11	10.68	9.01

For CGM range ≤ 80 mg/dL, the differences are reported in mg/dL instead of percent difference

Table 5. Agreement (%) of CGM-YSI paired points within YSI Glucose Ranges, calibrating three to four times a day, Abdomen insertion site.

YSI glucose ranges (mg/dL)	Number of paired CGM-YSI	Percent of CGM within 15/15% of YSI	Percent of CGM within 20/20% of YSI	Percent of CGM within 30/30% of YSI	Percent of CGM within 40/40% of YSI	Percent of CGM greater than 40/40% of YSI
Overall	7415	72.7	83.7	93.2	97.0	3.0
<40*	3	33.3	33.3	33.3	66.7	33.3
≥40-60*	618	79.6	91.1	96.1	97.9	2.1
>60-80*	1419	76.3	86.9	94.9	96.9	3.1
>80-180	3241	70.9	80.7	91.8	96.9	3.1
>180-300	1648	72.5	84.9	94.1	97.6	2.4
>300-350	325	71.4	84.9	94.5	98.2	1.8
>350-400	137	63.5	79.6	89.1	94.9	5.1
>400	24	33.3	41.7	54.2	66.7	33.3

* For YSI reference range ≤ 80 mg/dL, agreement was based on 15/20/30/40 mg/dL.
Note: CGM Readings are limited to 40-400 mg/dL.

Table 6. Agreement (%) of sensor-YSI paired points within YSI Glucose Ranges, calibrating every 12 hours. Abdomen insertion site

YSI glucose ranges (mg/dL)	Number of paired CGM-YSI	Percent of CGM within 15/15% of YSI	Percent of CGM within 20/20% of YSI	Percent of CGM within 30/30% of YSI	Percent of CGM within 40/40% of YSI	Percent of CGM greater than 40/40% of YSI
Overall	7432	68.1	79.0	90.2	96.3	3.7
<40*	3	33.3	33.3	66.7	100.0	0.0
≥40-60*	515	76.3	85.8	92.4	99.0	1.0
>60-80*	1349	70.5	82.5	92.8	98.8	1.2
>80-180	3158	64.9	76.5	89.0	95.9	4.1
>180-300	1895	68.9	78.9	90.2	95.4	4.6
>300-350	346	72.3	80.6	91.0	94.2	5.8
>350-400	132	72.0	79.5	87.9	93.2	6.8
>400	34	38.2	52.9	67.6	79.4	20.6

* For YSI reference range ≤ 80 mg/dL, agreement was based on 15/20/30/40 mg/dL. Note: CGM Readings are limited to 40-400 mg/dL.

Table 7. Agreement (%) of sensor-YSI paired points within CGM glucose ranges, calibrating three to four times a day. Abdomen insertion site,

CGM glucose ranges (mg/dL)	Number of paired CGM-YSI	Percent of CGM within 15/15% of YSI	Percent of CGM within 20/20% of YSI	Percent of CGM within 30/30% of YSI	Percent of CGM within 40/40% of YSI	Percent of CGM greater than 40/40% of YSI
Overall	7415	72.5	83.2	93.0	96.4	3.6
≥40-60*	620	80.0	87.7	94.7	97.9	2.1
>60-80*	1240	81.9	90.9	95.9	97.0	3.0
>80-180	3497	68.3	79.6	91.2	95.3	4.7
>180-300	1675	70.3	81.9	92.8	97.1	2.9
>300-350	266	77.8	88.0	96.6	99.2	0.8
>350-400	117	77.8	93.2	100.0	100.0	0.0

** For CGM reference range ≤ 80 mg/dL, agreement was based on 15/20/30/40 mg/dL.*

Table 8. Agreement (%) of sensor-YSI paired points within CGM glucose ranges, ,calibrating every 12 hours. Abdomen insertion site

CGM glucose ranges (mg/dL)	Percent of CGM within 15/15% of YSI	Percent of CGM within 20/20% of YSI	Percent of CGM within 30/30% of YSI	Percent of CGM within 40/40% of YSI	Percent of CGM greater than 40/40% of YSI	Percent of CGM within 15/15% of YSI
Overall	7432	68.3	78.9	90.2	95.5	4.5
≥40-60*	755	66.9	80.0	92.2	96.6	3.4
>60-80*	975	80.9	88.2	94.7	97.0	3.0
>80-180	3423	60.5	72.3	85.6	93.2	6.8
>180-300	1810	73.6	83.0	93.6	97.5	2.5
>300-350	342	83.6	90.6	98.0	100.0	0.0
>350-400	127	72.4	86.6	97.6	100.0	0.0

***** *For CGM reference range ≤ 80 mg/dL, agreement was based on 15/20/30/40 mg/dL.*

Table 9. The number and percentage of YSI values collected when CGM readings displayed 'Low' (less than 40 mg/dL); Calibrating three to four times a day, Abdomen insertion site.

		YSI mg/dL					
CGM readings	**CGM-YSI pairs**	**<55**	**<60**	**<70**	**<80**	**>80**	**Total**
'LOW'	Cumulative, n	8	13	22	23	0	23
'LOW'	Cumulative %	35%	57%	96%	100%	0%	

Table 10. The number and percentage of YSI values collected when CGM readings displayed 'High' (greater than 400 mg/dL); Calibrating three to four times a day, Abdomen insertion site.

		YSI mg/dL					
CGM readings	**CGM-YSI pairs**	**>340**	**>320**	**>280**	**>240**	**<240**	**Total**
'HIGH'	Cumulative, n	9	10	11	12	0	12
'HIGH'	Cumulative %	75%	83%	92%	100%	0%	

Table 11. The number and percentage of YSI values collected when CGM readings displayed 'Low' (less than 40 mg/dL); Calibrating every 12 hours, Abdomen insertion site.

		YSI mg/dL					
CGM readings	**CGM-YSI pairs**	**<55**	**<60**	**<70**	**<80**	**>80**	**Total**
'LOW'	Cumulative, n	16	23	27	45	0	45
'LOW'	Cumulative %	36%	51%	60%	100%	0%	

Table 12. The number and percentage of YSI values collected when CGM readings displayed 'High' (greater than 400 mg/dL); Calibrating every 12 hours, Abdomen insertion site.

		YSI mg/dL					
CGM readings	**CGM-YSI pairs**	**>340**	**>320**	**>280**	**>240**	**<240**	**Total**
'HIGH'	Cumulative, n	70	80	89	90	0	90
'HIGH'	Cumulative %	78%	89%	99%	100%	0%	

The following tables show the percentage of concurring CGM readings with YSI reference values. With ideal performance the CGM readings would match the YSI values, therefore the shaded boxes would ideally be 100 percent

Table 13. The concurrence of YSI values and CGM readings using YSI glucose ranges; Calibrating three to four times a day, Abdomen insertion site.

	Percent of matched pairs-in each CGM glucose range for each YSI glucose range CGM (mg/dL)											
YSI glucose ranges (mg/dL)	**Paired CGM-YSI (n)**	**<40**	**≥40-60**	**>60-80**	**>80-120**	**>120-160**	**>160-200**	**200-250**	**>250-300**	**>300-350**	**>350-400**	**>400**
A) <40	3	0.0%	33.3%	66.7%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
B) ≥40-60	631	2.1%	49.0%	43.9%	4.3%	0.8%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
C) >60-80	1429	0.7%	19.3%	54.3%	23.9%	1.7%	0.1%	0.0%	0.0%	0.0%	0.0%	0.0%
D) >80-120	1429	0.0%	2.0%	11.6%	67.2%	18.3%	0.8%	0.1%	0.0%	0.0%	0.0%	0.0%
E) >120-160	1271	0.0%	0.3%	1.3%	14.5%	64.5%	17.7%	1.4%	0.2%	0.0%	0.0%	0.0%
F) >160-200	981	0.0%	0.1%	0.1%	2.2%	21.4%	57.7%	17.1%	1.0%	0.3%	0.0%	0.0%
G) >200-250	689	0.0%	0.1%	0.0%	2.2%	4.1%	24.4%	54.6%	12.9%	1.7%	0.0%	0.0%
H) >250-300	520	0.0%	0.0%	0.2%	0.6%	0.6%	3.7%	32.9%	45.6%	12.9%	3.5%	0.2%
I) >300-350	328	0.0%	0.0%	0.0%	0.0%	0.3%	1.8%	11.0%	33.8%	38.7%	13.4%	0.9%
J) >350-400	142	0.0%	0.0%	0.0%	0.7%	1.4%	1.4%	3.5%	19.7%	36.6%	33.1%	3.5%
K) >400	27	0.0%	0.0%	0.0%	3.7%	3.7%	0.0%	18.5%	14.8%	18.5%	29.6%	11.1%

Table 14. The concurrence of YSI values and CGM readings using YSI glucose ranges; Calibrating every 12 hours, Abdomen only insertion site.

	Percent of matched pairs-in each CGM glucose range for each YSI glucose range CGM (mg/dL)											
YSI glucose ranges (mg/dL)	**Paired CGM-YSI (n)**	**<40**	**≥40-60**	**>60-80**	**>80-120**	**>120-160**	**>160-200**	**200-250**	**>250-300**	**>300-350**	**>350-400**	**>400**
A) <40	3	0.0%	33.3%	66.7%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
B) ≥40-60	538	4.3%	52.4%	33.3%	10.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
C) >60-80	1371	1.6%	30.0%	45.3%	22.8%	0.4%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
D) >80-120	1300	0.0%	3.2%	11.6%	60.0%	23.5%	1.7%	0.0%	0.0%	0.0%	0.0%	0.0%
E) >120-160	1327	0.0%	0.5%	1.3%	16.1%	61.4%	18.8%	2.0%	0.0%	0.0%	0.0%	0.0%
F) >160-200	1002	0.0%	0.3%	0.1%	3.7%	27.7%	48.2%	18.3%	1.6%	0.1%	0.0%	0.0%
G) >200-250	839	0.0%	0.0%	0.2%	3.1%	6.8%	20.3%	52.0%	15.6%	1.8%	0.2%	0.0%
H) >250-300	589	0.0%	0.2%	0.2%	0.8%	1.2%	5.1%	23.3%	49.6%	16.8%	2.2%	0.7%
I) >300-350	369	0.0%	1.1%	0.0%	0.8%	1.4%	2.4%	6.8%	23.0%	45.0%	13.3%	6.2%
J) >350-400	174	0.0%	0.6%	0.6%	0.0%	0.6%	1.1%	5.7%	9.2%	31.6%	26.4%	24.1%
K) >400	55	0.0%	7.3%	0.0%	0.0%	1.8%	1.8%	1.8%	7.3%	10.9%	30.9%	38.2%

Table 15. The concurrence of CGM readings and YSI values using CGM glucose ranges; Calibrating three to four times a day, Abdomen insertion site.

	Percent of matched pairs-in each YSI glucose range for each sensor glucose range YSI (mg/dL)											
CGM glucose ranges (mg/dL)	**Paired CGM-YSI (n)**	**<40**	**≥40-60**	**>60-80**	**>80-120**	**>120-160**	**>160-200**	**200-250**	**>250-300**	**>300-350**	**>350-400**	**>400**
A) <40	23	0.0%	56.5%	43.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
B) ≥40-60	620	0.2%	49.8%	44.5%	4.5%	0.6%	0.2%	0.2%	0.0%	0.0%	0.0%	0.0%
C) >60-80	1240	0.2%	22.3%	62.6%	13.4%	1.4%	0.1%	0.0%	0.1%	0.0%	0.0%	0.0%
D) >80-120	1555	0.0%	1.7%	22.0%	61.7%	11.8%	1.4%	1.0%	0.2%	0.0%	0.1%	0.1%
E) >120-160	1355	0.0%	0.4%	1.8%	19.3%	60.5%	15.5%	2.1%	0.2%	0.1%	0.1%	0.1%
F) >160-200	999	0.0%	0.0%	0.1%	1.2%	22.5%	56.7%	16.8%	1.9%	0.6%	0.2%	0.0%
G) >200-250	781	0.0%	0.0%	0.0%	0.3%	2.3%	21.5%	48.1%	21.9%	4.6%	0.6%	0.6%
H) >250-300	482	0.0%	0.0%	0.0%	0.0%	0.6%	2.1%	18.5%	49.2%	23.0%	5.8%	0.8%
I) >300-350	266	0.0%	0.0%	0.0%	0.0%	0.0%	1.1%	4.5%	25.2%	47.7%	19.5%	1.9%
J) >350-400	117	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	15.4%	37.6%	40.2%	6.8%
K) >400	12	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	8.3%	25.0%	41.7%	25.0%

Table 16. The concurrence of CGM readings and YSI values using CGM glucose ranges; Calibrating every 12 hours, Abdomen insertion site.

	Percent of matched pairs-in each YSI glucose range for each sensor glucose range YSI (mg/dL)											
CGM glucose ranges (mg/dL)	**Paired CGM-YSI (n)**	**<40**	**≥40-60**	**>60-80**	**>80-120**	**>120-160**	**>160-200**	**200-250**	**>250-300**	**>300-350**	**>350-400**	**>400**
A) <40	45	0.0%	51.1%	48.9%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
B) ≥40-60	755	0.1%	37.4%	54.4%	5.6%	0.8%	0.4%	0.0%	0.1%	0.5%	0.1%	0.5%
C) >60-80	975	0.2%	18.4%	63.7%	15.5%	1.7%	0.1%	0.2%	0.1%	0.0%	0.1%	0.0%
D) >80-120	1430	0.0%	3.8%	21.8%	54.5%	14.9%	2.6%	1.8%	0.4%	0.2%	0.0%	0.0%
E) >120-160	1474	0.0%	0.0%	0.3%	20.7%	55.3%	18.9%	3.9%	0.5%	0.3%	0.1%	0.1%
F) >160-200	966	0.0%	0.0%	0.0%	2.3%	25.8%	50.0%	17.6%	3.1%	0.9%	0.2%	0.1%
G) >200-250	819	0.0%	0.0%	0.0%	0.0%	3.3%	22.3%	53.2%	16.7%	3.1%	1.2%	0.1%
H) >250-300	544	0.0%	0.0%	0.0%	0.0%	0.0%	2.9%	24.1%	53.7%	15.6%	2.9%	0.7%
I) >300-350	342	0.0%	0.0%	0.0%	0.0%	0.0%	0.3%	4.4%	28.9%	48.5%	16.1%	1.8%
J) >350-400	127	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	1.6%	10.2%	38.6%	36.2%	13.4%
K) >400	90	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	4.4%	25.6%	46.7%	23.3%

Table 17. Agreement of Paired YSI-Sensor Values within 20%, 30% and 40% of YSI by sensor day, Abdomen Insertion Site

YSI glucose ranges (mg/dL)	Percent of CGM Within	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6
40-80	**20%**	64.4	67.2	61.7	63.5	76.1	79.2
	30%	79.3	89.7	80.2	84.7	88.0	89.6
	40%	88.5	97.4	92.6	94.1	94.6	94.8
>80-120	**20%**	58.4	62.2	72.8	71.4	66.2	76.4
	30%	76.9	82.8	87.0	85.0	81.5	89.3
	40%	84.4	92.2	94.4	89.3	90.4	93.6
>120-240	**20%**	68.2	80.5	79.6	78.1	75.0	77.6
	30%	85.7	93.0	97.7	91.8	88.9	87.5
	40%	92.0	97.0	95.5	97.1	95.3	91.6
>240-400	**20%**	70.0	77.9	80.3	77.1	76.9	70.8
	30%	90.0	93.8	94.4	91.6	85.9	88.9
	40%	96.0	97.3	98.6	95.2	91.0	93.1
Overall	**20%**	65.4	73.3	75.6	74.4	73.3	76.7
	30%	83.2	90.0	89.3	89.3	86.6	88.4
	40%	90.2	95.9	95.2	94.6	93.5	92.6

Alert Performance

Hypoglycemic alert performance within ±30 minutes of event

Alert performance is determined by CGM comparison with YSI within ± 30 minutes. For a 'hypoglycemic event' the YSI value is less than the tested CGM alert setting. 'CGM compared to YSI' reports the percent of times the CGM crosses the lower threshold when the YSI is below that threshold setting. 'YSI compare to CGM' reports the percent of time the YSI agrees with the CGM alerts.

Table 18. Both Threshold and Predictive alerts turned-on, Calibrating three to four times a day, Abdomen insertion site.

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	89.0	11.0	50.3	49.7
70	93.2	6.8	67.0	33.0
80	97.2	2.8	73.5	26.5
90	98.8	1.2	78.7	21.3
100	98.9	1.1	82.5	17.5

Table 19. Only Threshold alerts turned-on, Calibrating three to four times a day, Abdomen insertion site.

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	63.1	36.9	67.5	32.5
70	79.5	20.5	81.9	18.1
80	91.0	9.0	85.4	14.6
90	95.4	4.6	89.3	10.7
100	96.3	3.7	91.6	8.4

Table 20. Both Threshold and Predictive alerts turned-on, Calibrating every 12 hours, Abdomen insertion site.

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	86.3	13.7	39.7	60.3
70	92.5	7.5	61.8	38.2
80	96.5	3.5	72.2	27.8
90	97.3	2.7	76.9	23.1
100	98.1	1.9	78.8	21.2

Table 21. Only Threshold alerts turned-on, Calibrating every 12 hours, Abdomen insertion site.

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	70.2	29.8	51.4	48.6
70	83.1	16.9	74.5	25.5
80	89.8	10.2	83.5	16.5
90	94.9	5.1	87.6	12.4
100	95.4	4.6	87.8	12.2

Hyperglycemic alert performance within ±30 minutes of event

Alert performance is determined by CGM comparison with YSI within ± 30 minutes. For a 'hyperglycemic event' the YSI value is greater than the tested CGM alert value. 'CGM compared to YSI' reports the percent of times the CGM crosses the upper threshold when the YSI is above that threshold setting. 'YSI compare to CGM' reports the percent of time the YSI agrees with the CGM alerts.

Table 22. Both Threshold and Predictive alerts turned-on, Calibrating three to four times a day, Abdomen insertion site.

CGM alert setting (mg/dL)	CGM compared to YSI		YSI compared to CGM	
	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
	±30 Min	±30 Min	±30 Min	±30 Min
300	88.5	11.5	73.5	26.5
250	94.6	5.4	85.5	14.5
220	95.1	4.9	84.5	15.5
180	97.5	2.5	88.3	11.7

Table 23. Only Threshold alerts turned-on, Calibrating three to four times a day, Abdomen insertion site.

CGM alert setting (mg/dL)	CGM compared to YSI		YSI compared to CGM	
	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
	±30 Min	±30 Min	±30 Min	±30 Min
300	77.0	23.0	87.5	12.5
250	87.4	12.6	93.2	6.8
220	92.4	7.6	91.5	8.5
180	94.1	5.9	94.9	5.1

Table 24. Both Threshold and Predictive alerts turned-on, Calibrating every 12 hours, Abdomen insertion site.

CGM alert setting (mg/dL)	CGM compared to YSI		YSI compared to CGM	
	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
	±30 Min	±30 Min	±30 Min	±30 Min
300	89.1	10.9	73.2	26.8
250	94.5	5.5	84.5	15.5
220	94.3	5.7	85.2	14.8
180	94.6	5.4	88.6	11.4

Table 25. Only Threshold alerts turned-on, Calibrating every 12 hours, Abdomen insertion site.

CGM alert setting (mg/dL)	CGM compared to YSI		YSI compared to CGM	
	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
	±30 Min	±30 Min	±30 Min	±30 Min
300	82.0	18.0	84.7	15.3
250	87.9	12.1	92.3	7.7
220	90.1	9.9	92.8	7.2
180	91.1	8.9	94.6	5.4

Hypoglycemic alert performance within ±15 minutes of event

Alert performance is determined by CGM comparison with YSI within ± 15 minutes. For a 'hypoglycemic event' the YSI value is less than the tested CGM alert setting. 'CGM compared to YSI' reports the percent of times the CGM crosses the lower threshold when the YSI is below that threshold setting. 'YSI compare to CGM' reports the percent of time the YSI agrees with the CGM alerts.

Table 26. Both Threshold and Predictive alerts turned-on, Calibrating three to four times a day, Abdomen insertion site.

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 (%)
	±15 Min	±15 Min	±15 Min	±15 Min
60	79.2	20.8	35.7	64.3
70	87.1	12.9	54.1	45.9
80	93.8	6.2	63.1	36.9
90	96.4	3.6	67.8	32.2
100	96.7	3.3	72.7	27.3

Table 27. Only Threshold alerts turned-on, Calibrating three to four times a day, Abdomen insertion site.

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 (%)
	±15 Min	±15 Min	±15 Min	±15 Min
60	58.4	41.6	59.6	40.4
70	73.8	26.2	76.4	23.6
80	87.3	12.7	81.9	18.1
90	92.8	7.2	85.1	14.9
100	93.6	6.4	87.8	12.2

Table 28. Both Threshold and Predictive alerts turned-on, Calibrating every 12 hours, Abdomen insertion site.

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 (%)
	±15 Min	±15 Min	±15 Min	±15 Min
60	78.9	21.1	26.9	73.1
70	87.2	12.8	48.5	51.5
80	93.7	6.3	60.4	39.6
90	95.8	4.2	66.5	33.5
100	96.1	3.9	70.3	29.7

Table 29. Only Threshold alerts turned-on, Calibrating every 12 hours, Abdomen insertion site.

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 (%)
	±15 Min	±15 Min	±15 Min	±15 Min
60	66.2	33.8	44.9	55.1
70	78.0	22.0	68.0	32.0
80	87.3	12.7	78.8	21.2
90	92.7	7.3	83.3	16.7
100	93.3	6.7	84.4	15.6

Hyperglycemic alert performance within ±15 minutes of event

Alert performance is determined by CGM comparison with YSI within ± 15 minutes. For a 'hyperglycemic event' the YSI value is greater than the tested CGM alert value. 'CGM compared to YSI' reports the percent of times the CGM crosses the upper threshold when the

YSI is above that threshold setting. 'YSI compare to CGM' reports the percent of time the YSI agrees with the CGM alerts.

Table 30. Both Threshold and Predictive alerts turned-on, Calibrating three to four times a day, Abdomen insertion site.

CGM alert setting (mg/dL)	CGM compared to YSI		YSI compared to CGM	
	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
	±15 Min	±15 Min	±15 Min	±15 Min
300	82.6	17.4	63.2	36.8
250	90.9	9.1	79.0	21.0
220	93.0	7.0	79.6	20.4
180	95.0	5.0	83.1	16.9

Table 31. Only Threshold alerts turned-on, Calibrating three to four times a day, Abdomen insertion site.

CGM alert setting (mg/dL)	CGM compared to YSI		YSI compared to CGM	
	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
	±15 Min	±15 Min	±15 Min	±15 Min
300	70.9	29.1	80.3	19.7
250	83.3	16.7	89.9	10.1
220	89.4	10.6	88.6	11.4
180	91.6	8.4	91.8	8.2

Table 32. Both Threshold and Predictive alerts turned-on, Calibrating every 12 hours, Abdomen insertion site

CGM alert setting (mg/dL)	CGM compared to YSI		YSI compared to CGM	
	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
	±15 Min	±15 Min	±15 Min	±15 Min
300	85.6	14.4	65.6	34.4
250	91.1	8.9	78.3	21.7
220	91.6	8.4	80.4	19.6
180	92.0	8.0	83.7	16.3

Table 33. Only Threshold alerts turned-on, Calibrating every 12 hours, Abdomen insertion site

CGM alert setting (mg/dL)	CGM compared to YSI		YSI compared to CGM	
	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
	±15 Min	±15 Min	±15 Min	±15 Min
300	77.8	22.2	79.4	20.6
250	84.8	15.2	88.4	11.6
220	87.6	12.4	89.9	10.1
180	88.6	11.4	91.8	8.2

Precision Studies: Precisions studies were performed by inserting two Enlite sensors into the subjects' abdomen. The data from the precision studies were evaluated and found to be acceptable.

3. Subgroup Analyses

   Enlite sensor performance was evaluated within study population subgroups, such as frequent sampling participation group, diabetes type, age (18-21 years old, 22 years old and above), body mass index (BMI), baseline HbA1c (quartile groups), prior CGM experience, prior pump experience, and exercise activity (during in-clinic and home portions of the study).

   Although the study was not powered for analysis of subpopulations, no significant differences in performance were noted based on these subgroup analyses.

G100028

1. Safety Results

   The analysis of safety was based on the 50 subjects that participated in the study. Investigators were instructed to monitor the subjects throughout the course of the study for the occurrence of an adverse event.

   The safety data of the threshold suspend system were assessed by evaluation of the incidence of all Adverse Device Effects (ADEs), Serious Adverse Device Events (SADEs), and Unanticipated Adverse Device Effects (UADEs) experienced by study subjects. Adverse events (AEs) were listed in terms of severity and relationship to device.

   Adverse effects that occurred in G100028:

   There were a total of 29 adverse events reported by the sponsor - six (6) related to the study procedure, two (2) related to the device, one (1) related to both the device and the study procedure, and twenty (20) not related to the study procedure or the device. There were 21 subjects that had at least one (1) adverse event. All

adverse events were categorized as being mild or moderate in severity. The following is a summary of the reported adverse events:

Six (6) study related adverse events

- Blisters on toes due to exercising during study procedure
- Headache due to large carbohydrate intake
- Loss of dental filling during food intake
- Pain at IV site (2 events)
- Strained muscle due to exercise

Two (2) device related adverse events

- Bruising at sensor site
- Urine ketones (improper infusion tubing connection)

One (1) study and device related adverse event

- Bleeding at sensor site

Twenty (20) adverse events **not** related to study or device

- Fever
- Upper respiratory infection (2 events)
- Laceration to left eyebrow
- Sinus infection
- Right shoulder injury
- Nasal congestion
- Gastroenteritis (Stomach flu)
- Sore ribs
- Common cold (2 events)
- Herpes outbreak
- Nausea and body aches
- Sore throat
- Urinary tract infection
- Cough and congestion
- Tonsillitis (inflammation of tonsils)
- Strep throat
- Yeast infection
- Root canal

There were no reports of serious adverse events or unanticipated adverse device effects during the study.

A total of 134 induction sessions were performed for the 50 subjects; 69 with the Threshold Suspend (TS) set to 'ON' and 65 set to 'OFF'. Inductions were discontinued 9 times in the TS-ON and 8 times in the TS-OFF because of severe hypoglycemia (defined as blood glucose < 50 mg/dl by YSI). Ninety-eight (98)

studies were considered to be successful (hypoglycemia was induced and severe hypoglycemia did not occur).

2. Effectiveness Results

In this study, the pump successfully suspended insulin delivery when the sensor value fell below 70 mg/dL and resumed insulin delivery at the programmed basal rate after 2 hours. Although the Threshold Suspend resulted in temporary suspension of insulin delivery this action did not result in a difference in the number of hypoglycemia inductions that were stopped for severe hypoglycemia (blood glucose < 50 mg/dL) when compared to hypoglycemia inductions when the pump was not suspended. For the completed hypoglycemia inductions, there was not a clinically significant difference in the nadir glucose between the two treatment groups. The mean nadir glucose for TS-ON was 59.5 ± 5.72 and 57.6 ± 5.69 (p=0.015) for TS-OFF.

The actual patient experience with this device will likely be affected by the threshold level used and the quality of the sensor calibration. All calibrations in this study were done using the Bayer Contour glucose meter.

3. Subgroup Analyses
Threshold suspend performance was evaluated within study population subgroups, such as age (18-21 years old and 22 years and older).

Although the study was not powered for analysis of subpopulations, no significant differences in performance were noted based on these subgroup analyses.

E. Financial Disclosure

G100028
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 17 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.

G110131
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 36 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. 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 also 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 results of the pivotal clinical studies performed to support this submission establish a reasonable assurance of safety and effectiveness that the MiniMed 530G System can detect trends and track patterns and temporarily suspend the delivery of insulin when used as intended, as an adjuvant to blood glucose testing in subjects with diabetes mellitus.

The effectiveness of the Enlite sensor component was based on the performance evaluation of the Enlite Sensor compared to the blood glucose values measured by the reference method during in-clinic sessions spanning the wear period of the sensor (6 days). The performance data presented above (Tables 1 to 33) support the effectiveness conclusions and established the sensor performance across the claimed measuring range (40 to 400 mg/dL glucose), the precision, and the claimed calibration frequencies (calibrate every 12 hours or 3-4 times a day) of the 6 day wear period for the Enlite sensor. The performance data presented above also established the performance of the alarms and alerts of the Enlite sensor.

The effectiveness of the Threshold Suspend tool in correctly suspending insulin delivery at the set threshold was examined using the Sof-Sensor and the Medtronic Veo insulin pump (available outside of the United States). Though this system is not identical to the 530G system, this data can be extrapolated to support the safety and effectiveness of the 530G system for the following reasons.

The software for the Threshold Suspend tool is the same for the Veo pump and the 530G System. Though the Medtronic Sof-Sensor and the Enlite sensor are not identical, they operate using similar principles and fundamental scientific technology. The threshold suspend tool operates by simply turning off insulin delivery when the sensor value falls below a threshold set by the user (between 60and 90 mg/dL). Since the clinical study demonstrated that the threshold suspend software was effective at suspending insulin delivery based on Sof-Sensor values, a comparison of Sof-Sensor and Enlite performance at detecting various thresholds can enable extrapolation of how the Enlite may perform with such a tool. The hypoglycemic threshold alert

performance of the Sof-Sensor and the Enlite Sensor was evaluated over sensor wear. For example, the data in tables 34 and 35 demonstrate that the Enlite sensor performs similarly to the Sof-Sensor at a threshold of 70 mg/dL. The Sof-Sensor and Enlite-Sensor data are from separate sensor studies.

Table 34. Hypoglycemic alert performance with a threshold of 70 mg/dl within ±30 minutes of event; Only individual subject studies when the Threshold Alerts turned 'ON' (Threshold-only)

Sensor used (during the trial	CGM compared to Reference		Reference compared to CGM	
	Hypoglycemic events correctly detected (%)	Hypoglycemic events not detected (%)	Alerts verified by hypoglycemic events (%)	False alerts (%)
Sof-Sensor	68.8	31.2	82.6	17.4
Enlite Sensor	79.5	20.5	81.9	18.1

Table 35. Hypoglycemic alert performance with a threshold of 70 mg/dl within ±15 minutes of event; Only individual subject studies when the Threshold Alerts turned 'ON' (Threshold-only)

Sensor used (during the trial	CGM compared to Reference		Reference compared to CGM	
	Hypoglycemic events correctly detected (%)	Hypoglycemic events not detected (%)	Alerts verified by hypoglycemic events (%)	False alerts (%)
Sof-Sensor	64.2	35.8	76.4	23.6
Enlite Sensor	73.8	26.2	76.4	23.6

Key to Tables 34 and 35:

- The percent of hypoglycemic events correctly detected tells you how often a patient can expect the device to turn off when their actual blood glucose is below 70 mg/dL.
- The percent of hypoglycemic events not detected tells you how often a patient can expect the device not to turn off if their actual blood glucose is below 70 mg/dL.
- The percent of alerts verified by hypoglycemic events tells you if when a system suspends, how often the patient can expect their blood glucose to actually be below 70 mg/dL.
- The percent of false alerts tells you if when a system suspends, how often the patient can expect their blood glucose to be above 70 mg/dL.

Therefore, the data from the clinical studies supports the effectiveness of this device.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory data as well as on data collected in clinical studies conducted to support PMA approval as 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. There were no Serious Adverse Device Events (SADEs) or Unanticipated Adverse Device Effects (UADEs) reported during either of the clinical studies (G110131/A001 and G100028). 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, though all sensors were inspected for fracture after removal.

A minor risk of the CCM is that patients may need to perform unnecessary fingersticks to evaluate their blood glucose when the CGM gives false positive hypoglycemic and hyperglycemic readings or alerts. There is also a minor risk of skin irritation, inflammation, or infection due to either the sensor needle or the adhesive. However, CGM devices allow patients to measure the interstitial glucose at near continuous intervals to obtain a 24 hour picture of their glucose profile, especially during the night. Tracking and trending information is of value to patients and outweighs minor risks associated with fingersticks and the sensor.

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. 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 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 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 conducted to support PMA approval as described above.

The 530G device system 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 threshold to notify him or her that the sensor glucose is approaching (the case of the predictive) or has reached (in the case of the reactive) threshold of concern; the threshold for the Threshold Suspend tool 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 tool is an optional tool 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). Both the clinical and patient communities have expressed a strong desire for a threshold suspend tool to be available in the US. The Threshold Suspend tool is the first step toward a fully autonomous system. Although an automatic 2-hour suspension of insulin infusion was not shown to prevent severe hypoglycemia in a study where hypoglycemia was induced by exercise, this outcome is not unexpected because the sensor does not trigger pump suspension until the interstitial glucose is already in the hypoglycemic or near hypoglycemic range. In practice, patients with low blood glucose or glucose that is trending towards hypoglycemia would be expected to consume carbohydrates with or without manually adjusting the infusion rate of basal insulin. As would be expected, many patients who experienced mild hypoglycemia after exercise self-corrected after cessation of exercise whether the pump suspended or not. The greatest potential benefit of the Threshold Suspend may be for patients who develop a moderate hypoglycemia which is more likely to be mitigated by temporary suspension of insulin. The degree of this mitigation could not be determined in the study because of the limitations of the inductions and the variable time that subjects were followed once hypoglycemia occurred. Never-the-less, if used as intended and not as the primary method for the preventing hypoglycemia, the Threshold Suspend tool is likely to provide more benefit than risk.

The pump is unchanged from the previously approved model (Pardigm REVEL pump – P980022) with the exception of adding the Threshold Suspend tool, and some minor software differences. 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.
- 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 tool 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.

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

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 results of the pre-clinical testing and clinical trials to assess the performance of the MiniMed 530G System establish reasonable assurance that this system is safe and effective for its intended use when utilized in accordance with product labeling as an adjunct to information obtained from standard home glucose monitoring devices.

The benefits of using the System, as discussed above, outweigh the risks. In addition, the risks of using the System to determine diabetes therapy are mitigated by labelling.

The data presented in this submission support the use of this device in the intended use population and the potential achievement of clinically significant results in a significant portion of that patient population.

XIII. CDRH DECISION

CDRH issued an approval order on September 26, 2013. The final conditions of approval are cited in the approval order.

FDA issued a Warning Letter to Medtronic that listed violations observed during the preapproval inspection which occurred February through April, 2013. The Agency approved a variance plan that met the requirements set forth in Section 520(f)(2)(A) of the Federal Food, Drug, and Cosmetic Act and 21 C.F.R. 820(e)(2). Medtronic's variance plan provided methods to be used in, and the facilities and controls to be used for, the manufacture, packing, and storage of the MiniMed 530G system in lieu of the FDA's prescribed methods, facilities, and controls.

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.