SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Continuous Glucose Monitor (CGM) enabled insulin pump
Device Trade Name:	Paradigm REAL-Time Revel System
Device Procode:	MDS, OYC
Applicant's Name and Address:	Medtronic MiniMed 18000 Devonshire Street Northridge, CA, 91325
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P150019
Date of FDA Notice of Approval:	December 7, 2015

II. INDICATIONS FOR USE

Paradigm REAL-Time Revel insulin pump

The Paradigm REAL-Time Revel insulin pumps (MMT-523/MMT-723) are indicated for the continuous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin.

The Paradigm REAL-Time Revel system consists of the Paradigm MMT-523/MMT-723 insulin pumps, the Enlite glucose sensor (MMT-7008), and the MiniLink Transmitter (MMT-7703). Use of the Paradigm MMT-523/MMT-723 insulin pumps with the optional sensor and transmitter components is indicated for continuous or periodic monitoring of glucose levels in the fluid under the skin, and possible low and high blood glucose episodes in adults (ages 18 and older).

Enlite Sensor

The Enlite sensor (MMT-7008) is intended for use with the Paradigm REAL-Time Revel insulin pump systems (MMT-523/MMT-723) to continuously monitor glucose levels in persons with diabetes.

Glucose values provided by the Paradigm REAL-Time Revel system are not intended to be used directly for making therapy adjustments, but rather to provide an indication of when a fingerstick may be required. All therapy adjustments should be based on measurements obtained using a home glucose monitor and not on the sensor glucose readings provided by the Paradigm REAL-Time Revel system.

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 and to maintain contact with their healthcare professional. Successful insulin pump therapy requires sufficient vision or hearing to allow recognition of the pump signals and alarms.

- Do not expose your insulin pump to MRI equipment, diathermy, or other devices that generate very strong magnetic fields. The magnetic fields in the immediate vicinity of these devices can damage the part of the pump's motor that regulates insulin delivery, possibly resulting in over-delivery and severe hypoglycemia.

- Your pump must be removed and kept outside the room during magnetic resonance imaging (MRI) procedures.

- If your pump is inadvertently exposed to a strong magnetic field, discontinue use and contact our 24 Hour HelpLine for further assistance.

- Do not expose your transmitter to MRI equipment, diathermy devices, or other devices that generate strong magnetic fields. If your transmitter is inadvertently exposed to a strong magnetic field, discontinue use and contact the 24 Hour HelpLine for further assistance.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Paradigm REAL-Time Revel System labeling.

V. DEVICE DESCRIPTION

The Paradigm REAL-Time Revel system is comprised of an insulin pump, subcutaneously inserted glucose sensor, and transmitter which relays information from the glucose sensor to the insulin pump. Specifically, the system includes the following components:

Paradigm REAL-Time Revel Insulin Pump (MMT-523, MMT-723)

The Paradigm REAL-Time Revel insulin pump (models MMT-523, MMT-723) is an ambulatory, battery powered, rate-programmable infusion pump designed to deliver insulin from a reservoir. The medication reservoir is installed into the pump and a drive motor pushes a plunger into the reservoir to deliver patient determined basal rate profiles and patient selected bolus amounts of insulin into subcutaneous tissue through an infusion set.

In addition to delivery of insulin, the Paradigm REAL-Time Revel insulin pump can receive and display real-time glucose values received from a glucose sensor via a compatible transmitting device. When used in combination with a compatible Medtronic MiniMed transmitter and the Enlite glucose sensor, glucose sensor signals are transmitted from the transmitter to the Paradigm REAL-Time Revel Insulin Pump via radiofrequency (RF) telemetry. The transmitter physically connects to the glucose sensor and conducts

initial processing of sensor signals prior to direct transmission to the infusion pump. The pump further converts the digital sensor signals into sensor glucose values based on calibration with a commercially available blood glucose meter. Sensor glucose values can be displayed in real-time and are also stored into pump memory.

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.

The Paradigm REAL-Time Revel insulin pump is offered in two models, MMT-523 and MMT-723. The difference between models MMT-523 and MMT-723 is the size of the device and different compatible reservoir sizes. Model MMT-523 is compatible with a 1.8 ml reservoir whereas model MMT-723 can be used with either the 1.8mL or the 3.0 ml reservoir. Other than the size difference in the pump case housing and the inclusion of an additional electronic assembly (PCBA) rubber support, intended to provide physical support to the electronic assembly within the larger pump case housing, all other aspects of the pump (PCBA, drive motor, LCD, etc.) are the same between the two pump models.

The Paradigm REAL-Time Revel system was previously approved and is currently available for use with the Sof-sensor (MMT-7002, MMT-7003) glucose sensor which can be used for three (3) days. The only difference between this previously approved system and the Paradigm REAL-Time Revel System described here (P150019) is in the expanded use of the system to include the use of the Enlite Sensor (MMT-7008), which can be worn for up to six (6) days.

Enlite Sensor (MMT-7008)

The Enlite Sensor is a single-use disposable component, which is intended for use with Paradigm REAL-Time Revel insulin pump to continuously monitor glucose levels. The sensor is inserted into the subcutaneous tissue of the patient with the aid of a sensor insertion device. A rigid introducer needle aids in the insertion of the sensor into the subcutaneous tissue, and retracts into the polycarbonate hub of the insertion device after use. The sensor base remains outside of the body and is attached to the skin using an adhesive patch. The retractable needle is intended to prevent accidental needle sticks and allow for safe disposal once the sensor is in place. The sensor base connects to the transmitter (MiniLink transmitter (model MMT- 7703)), which communicates with the Paradigm REAL-Time Revel insulin pump. The Enlite Sensor is intended to be worn for up to six days.

MiniLink Real-Time System (MMT-7725)

The MiniLink Real-Time System consists of the MiniLink Transmitter (model MMT-7703), Charger (model MMT-7705), and Watertight Tester (model MMT-7726). The MiniLink Transmitter interfaces directly with the glucose sensor assembly. The MiniLink Transmitter provides power to the glucose sensor and measures the sensor signal current (ISIG) from the glucose sensor. The ISIG is an electrical current level that is proportional to the glucose level in the subcutaneous interstitial fluid of the patient. The ISIG is converted to a digital signal by the transmitter and is filtered to reduce noise. The digital

signal is then transmitted to a receiving device through a radio frequency link once every 5 minutes.

Optional Accessories Devices

The following optional accessory devices are compatible with the Paradigm REAL-Time Revel system:

Reservoirs and Infusion Sets	
MiniMed Quick Set Infusion Set	MMT-386, MMT-387, MMT-394, MMT-396, MMT-397
MiniMed Silhouette Infusion Set	MMT-368, MMT-369, MMT-370, MMT-377, MMT-378, MMT-381, MMT-382, MMT-383, MMT-384
MiniMed Mio Infusion Set	MMT-921, MMT-923, MMT-925, MMT-941, MMT-943, MMT-945, MMT-965, MMT-975
MiniMed Sure-T Infusion Set	MMT-862, MMT-864, MMT-866, MMT-874, MMT-876, MMT-886
Paradigm Polyfin Infusion Set	MMT-312S, MMT-312L
Paradigm Sof-Set Infusion Set	MMT-317, MMT-318 MMT-324, MMT-325
Paradigm Reservoir	MMT-326A MMT-332A
Additional Devices	
CareLink USB	MMT-7305
ComLink Communication Device	MMT-7304
CareLink Online (Personal)	MMT-7333
CareLink Pro	MMT-7335
Paradigm Remote Programmer	MMT-503
My Sentry System - Monitor - Outpost	MMT-9100 MMT-9101 MMT-9102
Enlite Serter	MMT-7510
Meter	
Bayer Contour NEXT LINK Meter	HMS-6203, HMS-6204, HMS-6207, HMS-9632, HMS-9633, HMS-9740

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the management of diabetes in persons requiring insulin. Management of diabetes can be achieved through a combination of methods and behaviors. Self-behaviors include healthy eating, taking clinically indicated medications as appropriate, and being physically active. Insulin delivery in persons with diabetes may occur by administration of insulin by injection (insulin pen or syringe) or by using other insulin infusion pumps as prescribed by a physician. Methods of controlling glucose levels (glycemic control) have been shown to reduce severe diabetes-related complications. One method of monitoring glycemic control includes periodic measurement of Hemoglobin A1c (HbA1c), which reflects average blood glucose levels over a three month period. Another method of monitoring glycemic control is self-

monitoring of blood glucose using glucose meters and test strips, which provides quantitative measurements of fingerstick blood glucose. This method provides glucose values at single points in time to patients and their healthcare providers and allows for more immediate treatment modifications than periodic HbA1c monitoring.

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

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

VII. MARKETING HISTORY

The Paradigm REAL-Time Revel system, for use with the Sof-sensor (MMT-7002, MMT-7003) continuous glucose sensor, has been in commercial distribution in the United States since 2010. However, this system has not been previously available with the Enlite continuous glucose sensor (MMT-7008). Although the Enlite sensor itself has been in commercial distribution in the United States since 2013 it has previously been approved for use only with a different continuous glucose monitoring system (MiniMed 530 system). The Enlite Sensor as a component of the MiniMed 530G system has been CE marked for commercial distribution in the European Union since 2011.

These devices have not been withdrawn from commercial distribution for any reason related to 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.

Potential device-related, non-serious events related to CGM or insulin pump use include:

- Local infection
- Skin inflammation
- Pain or discomfort
- Bleeding
- Bruising
- Itching
- Scarring or skin discoloration
- Allergic reactions to adhesives
- Sensor or needle fracture during insertion, wear or removal
- Hypoglycemia from over-delivery of insulin

- Hyperglycemia and ketosis possibly leading to ketoacidosis due to pump malfunction, or problems with the cannula, needle, or insulin infusion set tubing resulting in cessation of insulin delivery
- Catheter fracture or occlusion resulting in missed insulin dosing
- Failures of the infusion set or at infusion site resulting in inability to administer insulin
- Mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery

Sensor breakage with fragments retained under the skin and catheter fracture during infusion set insertion are potential procedure-related complication. However, based on post-market experience with this and similar devices, and the results observed in the clinical study, these events are rare and their severity does not raise major concerns.

One potential risk of using this device is that users might be inclined to use the CGM data in an unapproved way to determine their insulin dose or make therapy decisions. For these users, inaccurate glucose concentration data or alarms could result in inappropriate administration (including delayed administration) of insulin or ingestion of carbohydrates leading to the development or exacerbation of hypo- or hyperglycemia.

Like other insulin pumps, there is an inherent risk that patients who do not use the system as instructed (non-adherence) could harm themselves. Patients should be informed that sensor interstitial glucose values should not be used to make insulin dose decisions and that all threshold alerts and alarms should be confirmed with a blood glucose measurement.

The risks of actions taken based on false negative hyperglycemic readings include failure to administer or insufficient administration of insulin and inappropriate administration of extra carbohydrate. These inappropriate treatments could prolong or induce hyperglycemia. The risk of actions taken based on false negative hypoglycemic readings includes inappropriate administration of insulin or failure to administer or insufficient administration of extra carbohydrate. These inappropriate treatments could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death. False negative high alerts and low alerts and alarms will prevent the patient from having the opportunity to perform unplanned blood glucose tests and treat as instructed by their healthcare providers. There are similar additional possible risks if the system inaccurately calculates the rate of change of glucose.

The CGM component is to be used only for tracking and trending glucose levels. The risk related to either an inaccurate sensor value outside of the patient's normal range or a false alert or alarm is the risk of performing an unnecessary additional blood glucose test to confirm the erroneous sensor reading. The risk of medical harm may be mitigated through labeling which emphasizes that patients should confirm all CGM readings prior to making treatment decisions.

The risks of the device failing to alert an asymptomatic user to a high or low blood sugar is no greater than that associated with traditional blood glucose monitoring.

There are risks 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. Users may also need to perform fingersticks beyond what would otherwise be required for their diabetes management in order to calibrate the system.

For the specific adverse events that occurred in the clinical study, see Section X.- Summary of Primary Clinical Study, below.

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

Pre–clinical testing related to environmental exposure (including electromagnetic compatibility), mechanical functionality and drug stability, biocompatibility, sterility, packaging/shelf-life and shipping was performed on the MiniMed 530G insulin pump (models MMT-551, MMT-751), Enlite Sensor (MMT-7708) and MiniLink Transmitter (MMT-7703) and reviewed in P120010.

The only hardware difference between the MiniMed 530G insulin pump and the Paradigm REAL-Time Revel pump (models MMT-523, MMT-723) is that the MiniMed 530G Pump keypad overlay adds a green color to the circle around the ACT button. The addition of the green circle to the keypad overlay does impact requirements for hardware testing and would not impact testing results. All other aspects of the hardware (mechanical and electrical) between the MiniMed 530G and Paradigm REAL-Time Revel pumps are identical, and therefore the following studies conducted on the MiniMed 530G Pump apply to the Paradigm REAL-Time Revel pump (models MMT-523, MMT-723):

- environmental exposure (including electromagnetic compatibility)
- mechanical functionality and drug stability
- biocompatibility
- sterility
- packaging/shelf-life
- shipping

See the SSED for P120010 and P980022 for additional details on these laboratory studies, they are also summarized below:

I. Environmental Exposure

The following environmental exposure study (including electromagnetic compatibility) information was evaluated and approved as part of P120010 and is

applicable to this submission. See the Summary of Safety and Effectiveness Data for P120010 for additional information on these studies:

Paradigm® REAL-Time Revel™ Pump (MMT-523, MMT-723)
Representative insulin pumps were subjected to the following functional and environmental tests to ensure that these devices will continue to function normally even when exposed to extreme environmental conditions:

- 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
- 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 level pressure test

The following electromagnetic compatibility testing was performed to confirm that the device will 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

MiniLink® Transmitter (MMT-7703)

Thirty (30) MiniLink (MMT-7703) 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

The following electromagnetic compatibility testing was performed to confirm that the device will 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

Enlite Sensor

(MMT-7008) Sixty (60) 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

II. Mechanical Functionality and Drug Stability

Testing was conducted on the Paradigm REAL-Time Revel pump and provided to FDA for review in P980022/S031 and also in P120010. See the Summary of Safety and Effectiveness Data for P120010 for additional information on these studies. Insulin pumps were subjected to the following mechanical functionality and drug stability tests. The pump is for use with Humalog and Novlog insulins only, and drug stability testing was carried out only for these two insulins.

- Intermediate delivery volume accuracy
- Basal/bolus delivery volume accuracy
- Delivery Volume accuracy – environmental stress
- Deliver accuracy – reliability
- Drug stability and compatibility
- Insulin bioidentity and particulate tests
- Illumination test
- Extractables and leachables tests

III. Biocompatibility

The sponsor referenced biocompatibility testing from P120010 and P980022/S018 for the materials that comprise the Paradigm REAL-Time Revel system including the Pardigm Revel insulin pump, MiniLink Transmitter and Enlite Sensor. See the SSED for P120010 for additional information on these studies. All devices were found to be biocompatible for their intended use in accordance with ISO10993 - *Biological Evaluation of Medical Devices - Part 1: Evaluation and Testing.*

IV. Sterility

The sponsor referenced sterility testing from P120010. See the SSED for P120010 for additional information on these studies. The Enlite Sensor (MMT-7008) is a single use disposable device that is provided sterile and is intended to be worn for up to 6 days. The method employed for the sterilization of the Enlite Sensor is Electron Beam Sterilization. The sterilization process used to sterilize the sensor was validated according to the requirements per ISO 11137 *Sterilization of Health Care Products - Radiation.* All sterilized components meet the standards of IS0 11137 to assure a sterility assurance level (SAL) of 10-6. The sponsor also referenced sterility testing for the other sterile components of the system (reservoirs, tubing sets) that were approved under previous applications provided to the FDA. The remaining

system components (insulin pump, blood glucose meter, MiniLink transmitter, etc.) are provided non-sterile.

V. Packaging/Shelf-Life

Packaging and shelf-life testing of Paradigm REAL-Time Revel System was conducted in P120010. See the SSED for P120010 for additional information regarding packaging/shelf-life testing. The shelf-life of the Enlite Sensor (MMT-7008) was validated to be up to six months when stored at +2ºC to +30ºC according to the requirements of ISO 11607: *Packaging for Terminally Sterilized Medical Devices*, ASTM D 4169: *Standard Practice for Performance Testing of Shipping Containers and Systems* and ASTM F 1929: *Standard Test Method for Detecting Leaks in Porous Medical Packaging by Dye Penetration*. Packaging/shelf-life testing for the other components of the system (insulin pump, MiniLink Transmitter, etc.) were approved or cleared by FDA under previous applications.

VI. Software

The current software version for the Paradigm REAL-Time Revel insulin pump is v3.0B. There have been no changes to the pump application software since the most recent software update for this device and FDA review of those updates, which comprise version 3.0B (P980022/S153). Software verification and validation described in that submission were carried out in accordance with the *FDA Guidance: General Principles of Software Validation: Final Guidance for Industry and FDA Staff (January 11, 2002).* 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.

VII. Human Factors/Usability

The sponsor referenced human factors testing from previous submissions (as supplements to P980022 and in P120010). The testing considered device users, use environment, and user interfaces including device labeling and training. Human factors usability analysis was conducted in accordance to *FDA Guidance to Industry, and PMA and Design Control Reviewers, Medical Device Use-Safety: Incorporating Human Factors Engineering into Risk Management*. Detailed task analyses and usability assessments were conducted to confirm that the pump was designed to minimize the potential for user errors. The system was found acceptable for use. This information was evaluated and approved as part of previous submissions.

As the use of the Enlite Sensor with the Paradigm REAL-Time Revel System allows the system to be used with a six-day sensor as opposed to the previously approved 3-day sensor lifetime, the users have now been provided with an updated procedure on

re-starting the sensor to accommodate six days of use. Therefore, a human factors study was conducted to support the use of the Paradigm REAL-Time Revel System with the Enlite Sensor for six days. In this study, representative users were presented tasks associated with restarting the sensor after three days to allow a full six days of sensor use, and determining when to replace the sensor. Based on the evaluation, the updated procedure on re-starting the sensor to accommodate 6 day sensor use does not create additional usability risk.

B. Animal Studies

None.

C. Additional Studies

None.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The sponsor performed a clinical study to support the approval of P120010 to establish the accuracy of the Enlite Sensor when used in combination with the MiniMed 530G pump and CGM algorithm. The SSED for P120010 describes this clinical study, including study design, accountability of the study cohort, demographics and baseline parameters of the study population, adverse events and financial disclosure information. Data from the Enlite Sensor collected during this study was re-analyzed using the Paradigm Revel insulin pump CGM algorithm to establish a reasonable assurance of safety and effectiveness of the Enlite Sensor used as a component of the Paradigm REAL-Time Revel System.

Note that the MiniMed 530G pump uses a different algorithm relative to the Paradigm REAL-Time Revel pump to convert signals from the Enlite Sensor into glucose values; the two systems will produce different glucose values when provided with the same sensor and reference (calibration) inputs. However, each pump is capable of receiving signals from the Enlite Sensor sent through the MiniLink Transmitter. Therefore, evaluation of previously gathered Enlite Sensor data (G110131) using the Paradigm REAL-Time Revel pump (models MMT-523, MMT- 723) glucose sensor algorithm is an appropriate approach to characterize the performance of this system. This re-analysis provides the basis for the PMA approval decision. Key effectiveness outcomes are presented below in tables 1-9 and followed by a discussion of adverse events observed during the study.

Agreement of System Results with Reference Readings:

Agreement between the System and blood glucose values is characterized using paired System and established laboratory reference method (Yellow Springs Instruments Glucose analyzer) values. The System and reference results were compared by pairing the reference blood glucose value to a System glucose reading that occurred immediately after the reference was collected. The agreement of the System to blood glucose value was assessed by calculating the percentage of System readings that were within 15%,

20%, 30%, 40% and greater than 40% of the reference values. The total number of data pairs considered in this analysis was 7403 for calibration 3-4 times per day and 7467for calibration twice a day.

System Agreement to Reference within Reference Glucose Ranges: Tables 1-A and 1-B below are categorized within reference value ranges (in the first column) and outline how often a reading on the CGM matched the reference blood glucose range bin, with calibration three to four times per day or every 12 hours.

Table 1-A: System Agreement to Reference (Ref) within CGM Glucose Ranges (calibrating three to four times per day)

Ref glucose ranges (mg/dL)	Number of paired CGM-Ref	Percent of CGM within 15/15% of Ref	Percent of CGM within 20/20% of Ref	Percent of CGM within 30/30% of Ref	Percent of CGM within 40/40% of Ref	Percent of CGM greater than 40/40% of Ref
Overall	7403	66.8%	79.4%	92.1%	96.5%	3.5%
<40*	3	0%	33.3%	33.3%	66.7%	33.3%
≥40-60*	631	62.9%	78%	91.4%	97.3%	2.7%
>60-80*	1430	63.1%	78.6%	91.5%	95.5%	4.5%
>80-180	3225	66%	78%	91.1%	96.1%	3.9%
>180-300	1640	72.7%	83.2%	95.1%	97.7%	2.3%
>300-350	318	75.5%	86.5%	95.3%	98.7%	1.3%
>350-400	135	60.7%	74.8%	88.9%	97%	3%
>400	21	14.3%	23.8%	47.6%	85.7%	14.3%

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

Table 1-B: System Agreement to Reference (Ref) within CGM Glucose Ranges (calibrating every 12 hours)

Ref Glucose Range mg/dL	Number of paired System-Ref	Percent within 15/15% Ref	Percent within 20/20% Ref	Percent within 30/30% Ref	Percent within 40/40% Ref	Percent Greater than 40/40% Ref
Overall	7467	65.7%	77.1%	89.4%	95.3%	4.7%
<40*	3	0%	33.3%	33.3%	66.7%	33.3%
≥40-60*	543	61.5%	75.3%	87.1%	95%	5%
>60-80*	1376	64.1%	77%	88.7%	95.9%	4.1%
>80-180	3146	63%	74.5%	88.9%	95.1%	4.9%
>180-300	1885	71%	81%	91.6%	95.8%	4.2%
>300-350	345	73.9%	83.2%	90.4%	94.2%	5.8%
>350-400	136	71.3%	83.1%	89.7%	94.1%	5.9%
>400	33	42.4%	45.5%	69.7%	81.8%	18.2%

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

Note: CGM readings are within 40-400 mg/dL.

System Agreement to Reference within CGM Glucose Ranges: Tables 2-A and 2-B below are categorized with CGM glucose concentration ranges (in the first column) and outline how often a reading on the CGM matched the reference blood glucose reading, with calibration three to four times per day or every 12 hours.

Table 2-A: System Agreement to *Reference (Ref)* within CGM Glucose Ranges (calibrating three to four times per day)

CGM glucose ranges (mg/dL)	Number of paired CGM-Ref	Percent of CGM within 15/15% of Ref	Percent of CGM within 20/20% of Ref	Percent of CGM within 30/30% of Ref	Percent of CGM within 40/40% of Ref	Percent of CGM greater than 40/40% of Ref
Overall	7403	67.1%	80.1%	92%	96.5%	3.5%
≥40-60*	406	81%	90.9%	96.6%	98.8%	1.2%
>60-80*	1178	76.6%	88.7%	96.1%	97.4%	2.6%
>80-180	3703	60.1%	74.2%	88.8%	95.4%	4.6%
>180-300	1724	69.8%	82.9%	93.7%	97%	3%
>300-350	287	79.1%	87.8%	96.5%	99.7%	0.3%
>350-400	105	76.2%	83.8%	100%	100%	0%

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

Table 2-B: System Agreement to Reference (Ref) within CGM Glucose Ranges (calibrating every 12 hours)

CGM glucose ranges (mg/dL)	Number of paired CGM-Ref	Percent of CGM within 15/15% of Ref	Percent of CGM within 20/20% of Ref	Percent of CGM within 30/30% of Ref	Percent of CGM within 40/40% of Ref	Percent of CGM greater than 40/40% of Ref
Overall	7467	66.3%	77.7%	89.6%	95.4%	4.6%
≥40-60*	436	75%	83.5%	94%	97.7%	2.3%
>60-80*	1077	76.5%	88.7%	95.7%	97.7%	2.3%
>80-180	3575	57.7%	69.5%	84.6%	93%	7%
>180-300	1885	72%	82.7%	92.8%	96.9%	3.1%
>300-350	346	77.5%	89.6%	95.4%	99.4%	0.6%
>350-400	148	73%	86.5%	95.9%	100%	0%

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

Agreement of CGM to Reference When CGM Reads 'LOW' or 'HIGH':
The System reports glucose concentrations between 40 and 400 mg/dL. When the System determines the glucose level is below 40 mg/dL), the insulin pump screen displays "LOW". When the System determines that the glucose level is above 400 mg/dL the insulin pump screen displays "HIGH.". Because the System does not display glucose

values below 40 mg/dL or above 400 mg/dL, the comparisons to the actual blood glucose concentrations (as determined by the reference analyzer) when CGM is classified as "LOW" or "HIGH" are included separately in the following tables for calibration three to four times a day (Table 3A) or every 12 hours . (Table 3B) The tables includes the numbers and the cumulative percentages when reference values were less than certain glucose levels (for 'LOW'), and when reference values were greater than certain glucose levels (for 'HIGH').

Table 3-A. Number and percentage of reference (Ref) values when CGM readings are "Low" or "High" (calibrating three to four times per day).

		Ref mg/dL					
CGM readings	**CGM- Ref pairs**	**<55**	**<60**	**<70**	**<80**	**>80**	**Total**
'LOW'	Cumulative, n	0	0	0	0	0	0
'LOW'	Cumulative %	0%	0%	0%	0%	0%	
		Ref mg/dL					
CGM readings	**CGM- Ref pairs**	**>340**	**>320**	**>280**	**>240**	**<240**	**Total**
'HIGH'	Cumulative, n	16	20	23	23	0	23
'HIGH'	Cumulative %	70%	87%	100%	100%	0%	

Table 3-B. Number and percentage of Reference (Ref) values when CGM readings are "Low" or "High" (calibrating every 12 hours).

		Ref mg/dL					
CGM readings	**CGM- Ref pairs**	**<55**	**<60**	**<70**	**<80**	**>80**	**Total**
'LOW'	Cumulative, n	0	0	0	3	0	3
'LOW'	Cumulative %	0%	0%	0%	100%	0%	
		Ref mg/dL					
CGM readings	**CGM- Ref pairs**	**>340**	**>320**	**>280**	**>240**	**<240**	**Total**
'HIGH'	Cumulative, n	65	79	89	90	0	90
'HIGH'	Cumulative %	72%	88%	99%	100%	0%	

Concurrence of System and Laboratory Reference Values:

The percentage of concurring CGM readings and reference values are presented on the following page in Tables 4-A and 4-B. These tables are categorized by each reference glucose range (first column) and describe for each range of reference (true) glucose readings the percentage of paired CGM values that fell within the same glucose range (shaded) or in glucose ranges above and below the paired reference readings.

Table 4-A. Concurrence of Reference (Ref) values and System Readings (calibrating three to four times per day).

Ref (mg/dL)	Percent of Matched Pairs-in Each CGM Glucose Range for Each Ref Glucose Range											
	CGM (mg/dL)											
	Number of Paired CGM- Ref	<40	≥40-60	>60-80	>80-120	>120-160	>160-200	>200-250	>250-300	>300-350	>350-400	>400
<40	3	0.0%	33.3%	66.7%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
≥40-60	631	0.0%	34.1%	53.2%	11.6%	1.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
>60-80	1430	0.0%	12.1%	48.1%	37.0%	2.8%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
>80-120	1423	0.0%	1.2%	9.5%	63.4%	24.5%	1.3%	0.1%	0.0%	0.0%	0.0%	0.0%
>120-160	1265	0.0%	0.0%	1.1%	12.9%	62.5%	21.3%	2.1%	0.2%	0.0%	0.0%	0.0%
>160-200	971	0.0%	0.0%	0.2%	1.3%	19.1%	56.0%	22.0%	1.1%	0.2%	0.0%	0.0%
>200-250	689	0.0%	0.0%	0.1%	2.0%	3.3%	24.1%	54.6%	13.9%	1.9%	0.0%	0.0%
>250-300	518	0.0%	0.0%	0.0%	0.8%	0.2%	2.3%	29.5%	46.1%	16.8%	4.1%	0.2%
>300-350	327	0.0%	0.0%	0.0%	0.0%	0.0%	1.2%	8.3%	36.4%	40.7%	10.7%	2.8%
>350-400	142	0.0%	0.0%	0.0%	0.7%	0.7%	0.7%	2.1%	26.8%	31.7%	32.4%	4.9%
>400	27	0.0%	0.0%	0.0%	0.0%	7.4%	0.0%	3.7%	29.6%	25.9%	11.1%	22.2%

Table 4-B. Concurrence of Reference (Ref)values and System Readings (calibrating every 12 hours).

Ref (mg/dL)	Percent of Matched Pairs-in Each CGM Glucose Range for Each Ref Glucose Range											
	CGM (mg/dL)											
	Number of Paired CGM- Ref	<40	≥40-60	>60-80	>80-120	>120-160	>160-200	>200-250	>250-300	>300-350	>350-400	>400
<40	3	0.0%	33.3%	33.3%	33.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
≥40-60	543	0.0%	30.8%	52.3%	14.9%	2.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
>60-80	1379	0.2%	17.8%	46.1%	33.8%	2.1%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
>80-120	1292	0.0%	1.3%	10.2%	55.8%	29.6%	2.9%	0.2%	0.0%	0.0%	0.0%	0.0%
>120-160	1327	0.0%	0.2%	1.0%	13.5%	61.2%	21.0%	3.1%	0.1%	0.0%	0.0%	0.0%
>160-200	991	0.0%	0.3%	0.1%	2.2%	21.3%	52.7%	21.5%	1.6%	0.3%	0.0%	0.0%
>200-250	838	0.0%	0.0%	0.0%	2.3%	7.0%	19.1%	53.2%	16.1%	1.7%	0.6%	0.0%
>250-300	586	0.0%	0.0%	0.2%	0.9%	1.0%	5.1%	27.1%	43.5%	18.1%	3.6%	0.5%
>300-350	372	0.0%	0.0%	0.8%	0.5%	2.2%	2.7%	5.4%	24.5%	41.7%	15.1%	7.3%
>350-400	174	0.0%	0.0%	1.1%	0.0%	0.6%	2.3%	4.0%	6.3%	34.5%	29.3%	21.8%
>400	55	0.0%	0.0%	7.3%	0.0%	0.0%	3.6%	0.0%	7.3%	14.5%	27.3%	40.0%

Evaluation of Accuracy:

Accuracy between matched pairs was also estimated by calculating the percent difference between the System reading and the reference value. The System and reference values

were compared by pairing the System reading that fell immediately after the reference value was collected.

The mean relative difference is the average of all positive and negative percent differences between the two devices and demonstrates whether the System reads higher or lower on average than the reference at each glucose range.

Another estimate used to evaluate the accuracy of the System is the absolute percent difference. The absolute percent difference provides the percent difference or "distance" between the System and reference values, but does not demonstrate whether the System is reading, on average, higher or lower than the reference. The mean absolute percent difference is the average "distance" (regardless if positive or negative) between System readings and reference values.

These accuracy measures are summarized in Tables 5-A and 5-B below. These tables are categorized by CGM glucose range (first column) and demonstrate that the System reads, on average, 2.20% lower than the reference (Mean relative difference) and with an average 14.51% absolute difference (Mean absolute relative difference) relative to the reference values when calibrating three to four times per day. When calibrating every 12 hours, the system reads, on average, 0.20% lower (Mean relative difference) than the reference and with an average 16.08% absolute difference (Mean absolute relative difference) relative to the reference values.

Table 5-A. CGM difference to Reference (Ref) within CGM glucose ranges, calibrating three to four times per day.

CGM glucose ranges (mg/dL)	Number of paired CGM- Ref	Mean relative difference (%)	Median relative difference (%)	Mean absolute relative difference (%)	Median absolute relative difference (%)
Overall	7403	-2.20	-4.29	14.51	11.11
40-60*	406	5.76	4.15	8.60	5.73
61-80*	1178	-3.48	-6.37	11.39	9.60
81-180	3703	-4.12	-5.90	15.43	11.80
181-300	1724	0.66	-0.55	12.31	9.81
301-350	287	-2.55	-2.28	9.50	6.62
351-400	105	-7.58	-6.74	9.63	7.98

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

Table 5-B. CGM difference to Reference (Ref) within CGM glucose ranges, calibrating every 12 hours.

CGM glucose ranges (mg/dL)	Number of paired CGM- Ref	Mean relative difference (%)	Median relative difference (%)	Mean absolute relative difference (%)	Median absolute relative difference (%)
Overall	7403	-0.20	-3.72	16.08	11.05
40-60*	406	9.81	7.60	12.07	8.40
61-80*	1178	0.77	-4.15	13.04	8.00
81-180	3703	-2.49	-5.88	17.38	12.50

181-300	1724	-0.44	-2.13	12.11	8.96
301-350	287	-2.19	-1.31	9.83	7.76
351-400	105	-7.37	-6.78	10.68	9.43

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

Tables 6-A and 6-B below are categorized within reference glucose value ranges (first column) and show that half of the time (Median relative difference) the System read less than 4.49% higher than the reference blood glucose values and that half of the time the System read less than 11.45% different than reference blood glucose values for calibration three to four times per day. For calibration twice a day, the System read less than 4.49% higher than the reference blood glucose values and that half of the time the System read less than 11.45% different than reference blood glucose values

Table 6-A: System Differences to Reference (Ref) within Reference Glucose Ranges (calibrating three to four times per day)

Ref glucose ranges (mg/dL)	**Number of paired CGM- Ref**	**Mean relative difference (%)**	**Median relative difference (%)**	**Mean absolute relative difference (%)**	**Median absolute relative difference (%)**
Overall	7403	6.27	4.49	15.57	11.45
<40*	3	30.85	32.65	30.85	32.65
40-60*	631	12.60	11.65	13.94	11.70
61-80*	1430	10.37	9.10	14.34	11.40
81-180	3225	5.10	4.68	13.55	10.45
181-300	1640	-1.61	-1.66	11.65	8.91
301-350	318	-6.25	-5.82	10.68	8.59
351-400	135	-12.49	-10.80	13.50	10.86
>400	21	-29.76	-31.04	29.76	31.04

***** *For reference range ≤ 80 mg/dL, the differences in mg/dL are included instead of relative difference (%).*

Note: CGM readings are within 40 to 400 mg/dL.

Table 6-B: System Differences to Reference (Ref) within Reference Glucose Ranges (calibrating every 12 hours).

Ref glucose ranges (mg/dL)	**Number of paired CGM- Ref**	**Mean relative difference (%)**	**Median relative difference (%)**	**Mean absolute relative difference (%)**	**Median absolute relative difference (%)**
Overall	7467	5.24	3.87	16.15	11.36
<40*	3	33.18	33.65	33.18	33.65
40-60*	543	13.43	11.40	15.22	11.85
61-80*	1376	7.77	5.75	13.90	10.40
81-180	3146	5.66	5.56	14.86	11.12
181-300	1885	-1.92	-0.54	12.46	9.13
301-350	345	-6.69	-3.53	12.38	7.96
351-400	136	-11.44	-7.53	12.83	8.44
>400	33	-27.54	-22.91	27.54	22.91

***** *For reference range ≤ 80 mg/dL, the differences in mg/dL are included instead of relative difference (%).*
Note: CGM readings are within 40 to 400 mg/dL.

Low and High Glucose Alerts: The System has programmable High and Low Glucose Threshold and Predictive Alerts that can be changed by the user. The labeling instructs the user to consult with their doctor to determine what settings would be best for them.

To assess the ability of the System to detect high and low glucose levels System results were compared to reference results at low and high blood glucose levels and it was determined if the alert may have sounded. The System and reference readings were compared by pairing the System reading that occurred immediately after the reference reading was collected.

Low Glucose (Hypoglycemic) Alert: Estimates of how well the adjustable Low Glucose Alert performed are presented below in Tables 7-A through 7-F, with the following definitions of terms used in the tables:

Hypoglycemia Alert Rate:
The Alert Rate shows how often the alert was right or wrong. The *hypoglycemic events correctly detected* rate is the % of times the device alarmed when the blood glucose level was at or below the alert setting within 15 minutes before or after the device alarmed. The *false alert* rate is the % of times the device alarmed when the blood glucose level was above the alert setting within 15 minutes before or after the device alarmed.

Hypoglycemia Detection Rate:
The Detection Rate shows how often the device recognized and alerted that there was an episode of hypoglycemia or how often it missed such an event. The *alerts verified by hypoglycemic events* rate is the % of times the blood glucose level was at or below the alert setting and the device alarmed within 15 minutes before or after the blood glucose was at or below the alert settings. The *hypoglycemia events not detected* rate is the % of times the blood glucose was at or below the alert setting, but the device did not alarm within 15 minutes before or after the blood glucose was at or below the alert setting.

Table 7-A: Both threshold and predictive alerts turned-on (calibrating three to four times per day).

CGM alert setting (mg/dL)	Hypoglycemic events correctly detected (%)	Hypoglycemic events not detected (%)	Alerts verified by hypoglycemic events (%)	False alerts (%)
60	58.1	41.9	37.7	62.3
70	74	26	58.2	41.8
80	85.6	14.4	67.7	32.3
90	91.3	8.7	71.5	28.5
100	93.5	6.5	76	24

Table 7-B: Only threshold alerts turned-on (calibrating three to four times per day).

CGM alert setting (mg/dL)	Hypoglycemic events correctly detected (%)	Hypoglycemic events not detected (%)	Alerts verified by hypoglycemic events (%)	False alerts (%)
60	43	57	65.9	34.1
70	55.7	44.3	79.3	20.7
80	75.5	24.5	84.7	15.3
90	86.3	13.7	87.9	12.1
100	88.7	11.3	90.2	9.8

Table 7-C: Only predictive alerts turned-on (calibrating three to four times per day).

CGM alert setting (mg/dL)	Hypoglycemic events correctly detected (%)	Hypoglycemic events not detected (%)	Alerts verified by hypoglycemic events (%)	False alerts (%)
60	55.7	44.3	39.7	60.3
70	72.1	27.9	59.6	40.4
80	83.9	16.1	68.5	31.5
90	89.6	10.4	72.7	27.3
100	91.9	8.1	77.4	22.6

Table 7-D: Both threshold and predictive alerts turned-on (calibrating every 12 hours).

CGM alert setting (mg/dL)	Hypoglycemic events correctly detected (%)	Hypoglycemic events not detected (%)	Alerts verified by hypoglycemic events (%)	False alerts (%)
60	66.1	33.9	31.8	68.2
70	78.2	21.8	52.6	47.4
80	86.7	13.3	64.9	35.1
90	90.7	9.3	71.4	28.6
100	92.6	7.4	74.3	25.7

Table 7-E: Only threshold alerts turned-on (calibrating every 12 hours).

CGM alert setting (mg/dL)	Hypoglycemic events correctly detected (%)	Hypoglycemic events not detected (%)	Alerts verified by hypoglycemic events (%)	False alerts (%)
60	40.7	59.3	48.3	51.7
70	61.8	38.2	71.9	28.1
80	76.5	23.5	81.6	18.4

90	85.1	14.9	86	14
100	88.4	11.6	87.2	12.8

Table 7-F: Only predictive alerts turned-on (calibrating every 12 hours).

CGM alert setting (mg/dL)	Hypoglycemic events correctly detected (%)	Hypoglycemic events not detected (%)	Alerts verified by hypoglycemic events (%)	False alerts (%)
60	64.4	35.6	34.5	65.5
70	75.9	24.1	55.2	44.8
80	85.1	14.9	67	33
90	88.6	11.4	73	27
100	91	9	75.7	24.3

High Glucose Alert: Estimates of how well the adjustable High Glucose Alert performed are presented below in Tables 8-A through 8-F with the following definitions of the terms used in the tables:

Hyperglycemia Alert Rate:
The Alert Rate shows how often the alert was right or wrong. The *hyperglycemic events correctly detected* rate is the % of times the device alarmed when the blood glucose level was at or above the alert setting within 15 minutes before or after the device alarmed. The *false alert* rate is the % of times the device alarmed when the blood glucose level was below the alert setting within 15 minutes before or after the device alarmed.

Hyperglycemia Detection Rate:
The Detection Rate shows how often the device recognized and alerted that there was an episode of hyperglycemia or how often it missed such an event. The *hyperglycemia events not detected* rate is the % of times the blood glucose level was at or above the alert setting and the device alarmed within 15 minutes before or after the blood glucose was at or above the alert settings. The *alerts verified by hyperglycemic events* rate is the % of times the blood glucose was at or above the alert setting, but the device did not alarm within 15 minutes before or after the blood glucose was at or above the alert setting.

Table 8-A: Both threshold and predictive alerts turned-on (calibrating three to four times per day).

CGM alert setting (mg/dL)	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
300	84.6	15.4	62.3	37.7
250	92.9	7.1	78	22
220	93	7	77.5	22.5
180	95.5	4.5	81.3	18.7

Table 8-B: Only threshold alerts turned-on (calibrating three to four times per day).

CGM alert setting (mg/dL)	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
300	68.5	31.5	76.3	23.7
250	86.2	13.8	89.3	10.7
220	89.1	10.9	87.3	12.7
180	92.5	7.5	89.6	10.4

Table 8-C: Only predictive alerts turned-on (calibrating three to four times per day).

CGM alert setting (mg/dL)	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
300	81.7	18.3	66.2	33.8
250	89.9	10.1	80.2	19.8
220	91	9	80.2	19.8
180	93	7	84.4	15.6

Table 8-D: Both threshold and predictive alerts turned-on (calibrating every 12 hours).

CGM alert setting (mg/dL)	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
300	86.1	13.9	66.2	33.8
250	89.7	10.3	77.4	22.6
220	92	8	79.3	20.7
180	93.8	6.2	81.8	18.2

Table 8-E: Only threshold alerts turned-on (calibrating every 12 hours).

CGM alert setting (mg/dL)	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
300	77.8	22.2	78.3	21.7
250	83.3	16.7	87.6	12.4
220	87.7	12.3	88.7	11.3
180	90.4	9.6	89.6	10.4

Table 8-F: Only predictive alerts turned-on (calibrating every 12 hours).

CGM alert setting (mg/dL)	Hyperglycemic events correctly detected (%)	Hyperglycemic events not detected (%)	Alerts verified by hyperglycemic events (%)	False alerts (%)
300	84.3	15.7	69.6	30.4
250	87.8	12.2	80.3	19.7
220	90	10	81.9	18.1
180	91.5	8.5	84.8	15.2

Calibration Stability:

The System must be calibrated every 12 hours. To demonstrate performance of the System over a 12-hour calibration period, Sensors were evaluated to verify that performance remains consistent over the 12-hour calibration period. Systems were evaluated in 2-hour increments after calibration and performance was estimated at each 2-hour interval and stratified by glucose concentrations by calculating the percentage of System readings within 15 mg/dL or 15%, 20 mg/dL or 20%, 30 mg/dL or 30%, 40 mg/dL or 40% and greater than 40 mg/dL or 40% of the reference values in Table 9.

Table 9: Accuracy for 12 hours following calibration

Time from Calibration	Number of paired Ref - System points	Percent within ± 15% (± 15 mg/dL)	Percent within ± 20% (± 20 mg/dL)	Percent within ± 30% (± 30 mg/dL)	Percent within ± 40% (± 40 mg/dL)	Percent > ±40% (± 40 mg/dL)
0–2 hours	1571	63.3	77.7	91.7	97.3	2.7
2–4 hours	1687	61.6	76.8	91.5	96.9	3.1
4–6 hours	1219	61.9	72.9	87.2	95.2	4.8
6–8 hours	454	55.3	67.4	81.5	90.7	9.3
8–10 hours	360	48.6	63.3	77.2	83.6	16.4
10–12 hours	311	54.7	63.7	83.9	87.5	12.5

Adverse Events

Twenty-two adverse events were reported to the sponsor during the study of Enlite Sensor accuracy (G110131), 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.

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.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness of the Enlite Sensor as a component of the Paradigm REAL-Time Revel System was based on the performance evaluation of the Enlite Sensor functioning as component of this system 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 1-9) support the effectiveness conclusions and established sensor performance across the claimed measuring range (40 to 400 mg/dL glucose) 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 when used as a component of the Paradigm REAL-Time Revel System. The performance data presented above also established the performance of the alarms and alerts of the Enlite sensor when used as a component of the Paradigm REAL-Time Revel System.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory data as well as on data collected in the clinical study (G110131). For study-related events, see Section X. Summary of Primary Clinical Study, above.

Potential device-related, non-serious events related to CGM or insulin pump use include:

- Local infection
- Skin inflammation
- Pain or discomfort
- Bleeding
- Bruising
- Itching
- Scarring or skin discoloration
- Allergic reactions to adhesives
- Sensor or needle fracture during insertion, wear or removal
- Hypoglycemia from over-delivery of insulin
- Hyperglycemia and ketosis possibly leading to ketoacidosis due to pump malfunction, or problems with the cannula, needle, or insulin infusion set tubing resulting in cessation of insulin delivery
- Catheter fracture or occlusion resulting in missed insulin dosing
- Failures of the infusion set or at infusion site resulting in inability to administer insulin
- Mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery

Sensor breakage with fragments retained under the skin and catheter fracture during infusion set insertion are potential procedure-related complication. However, based on post-market experience with this and similar devices, and the results observed in the clinical study, these events are rare and their severity does not raise major concerns.

One potential risk of using this device is that users might be inclined to use the CGM data in an unapproved way to determine their insulin dose or make therapy decisions. For these users, inaccurate glucose concentration data or alarms could result in inappropriate administration (including delayed administration) of insulin or ingestion of carbohydrates leading to the development or exacerbation of hypo- or hyperglycemia.

A pump malfunction could lead to clinically significant hypoglycemic event, ketosis or ketoacidosis. A patient should respond with carbohydrate, insulin therapy, hydration, or other medical assistance as necessary. If unaddressed, severe hypoglycemia, severe hyperglycemia and ketoacidosis can result in serious harm and death.

The risks of actions taken based on false negative hyperglycemic readings include failure to administer or insufficient administration of insulin and inappropriate administration of extra carbohydrate. These inappropriate treatments could prolong or induce hyperglycemia. The risk of actions taken based on false negative hypoglycemic readings includes inappropriate administration of insulin or failure to administer or insufficient administration of extra carbohydrate. These inappropriate treatments could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death. False negative high alerts and low alerts and alarms will prevent the patient from having the opportunity to perform unplanned blood glucose tests and treat as instructed by their healthcare providers. There are additional possible risks if the system inaccurately calculates the rate of change of glucose.

Risks of actions taken based on false positive hyperglycemic readings include inappropriate or excessive administration of insulin and failure to treat hypoglycemia. These inappropriate treatments could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death. The risks of actions taken based on false positive hypoglycemic readings include failure to administer insulin and failure to treat hyperglycemia. False positive high alerts and low alerts and alarms may increase the number of unplanned blood glucose checks; and disrupt patient activity and sleep. If the false positive rate is too high it can result in 'alarm fatigue' and patients may deactivate these alerts/alarms.

The risks of the device failing to alert an asymptomatic user to a high or low blood sugar is no greater than that associated with traditional blood glucose monitoring.

The CGM component is to be used only for tracking and trending glucose levels. The risk related to either an inaccurate sensor value outside of the patient's normal range or a false alert or alarm is the risk of performing an unnecessary additional blood glucose test to confirm the erroneous sensor reading. The risk of medical harm may be mitigated through labeling which emphasizes that patients should confirm all CGM readings prior to making treatment decisions.

The risks of using this device are similar to the risks associated with the separate components of the system.

C. Benefit-Risk Conclusions

The probable benefits of the CGM component of the device are based on data collected in a clinical study conducted to support PMA approval of the Enlite sensor as described above and in P120010.

The Paradigm REAL-Time Revel 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 a subcutaneous glucose

sensor and tracking and trending information to supplement traditional blood glucose measurements.

The continuous glucose monitoring component of the Paradigm REAL-Time Revel System has been updated to use a new glucose sensor (Enlite Sensor) relative to the previous sensor (Sof-Sensor) originally approved for use with this device (P980022/S031, P980022/S089). The Enlite sensor has an extended wear period relative to the Sof-Sensor (6 days vs. 3 days). The CGM is intended to supplement self-monitoring of blood glucose to track and trend interstitial glucose levels as estimates of glucose excursions in the blood. The system provides continuous measurements of glucose in the tissue every 5 minutes for up to seven days for each sensor. 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.

Other benefits of the CGM component of the system include:

- Provide information regarding patterns of glycemic excursions throughout the day and night when patients may be unable to test their blood glucose
- The alert/alarm functions aid in the in the early detection of episodes of hyperglycemia and hypoglycemia (which may facilitate both acute and long-term therapy adjustments that may minimize episodes of hyper and hypoglycemia)
- Timely estimation of both point blood glucose concentration and rate of change in blood in addition to providing tracking and trending of glucose patterns both in the short term and over several days by this device. This information will aid in the prevention of extremes of glycemia.
- The results from this device will provide more detailed information regarding patterns of glycemic trends than is possible with traditional self-blood glucose testing with meters and that this information, combined with traditional glucose monitoring, will aid in the management of diabetes

The insulin pump component of the system is indicated for continuous subcutaneous insulin infusion to assist patients in the management of their diabetes by allowing for various basal and bolus delivery settings. Other benefits of the pump component include the following:

- Ability to administer insulin frequently without repeated injection
- Ability to set different basal rates through the day to better match basal insulin requirements which may fluctuate during the course of the day
- Ability to calculate active insulin remaining from previous boluses to avoid “insulin stacking”, which can lead to hypoglycemia
- Ability to administer bolus doses over an extended time
- Ability for patient to calculate appropriate bolus insulin doses based on their individual needs

The functions of this device are not feasible using traditional blood glucose monitoring and insulin self-injections as blood glucose meters only provide information about discrete, intermittent blood glucose levels. This device provides information regarding

patterns of glycemic excursions continuously throughout the day and night when patients might be unable to test their blood glucose using traditional methods. The device also allows for extended bolus administration, the administration of basal insulin rates to be modified throughout the day and significantly simplifies the determination of active insulin remaining from previous boluses.

Ease of use features that enhance the benefits of the system includes the following:

- Single user interface
- Convenience to user – one less device to carry
- Extended sensor wear period relative to previously approved version of the device
- Increased convenience of CGM use from less frequent sensor changes and corresponding increased incentive to overall increased CGM use, providing a greater availability of the benefits of CGM

Risks of the CGM and Sensor include the following:

- Sensor error resulting in incorrect glucose readings
- The CGM component is to be used only for tracking and trending. The risk related to either an inaccurate sensor value outside of the patient's normal range or a false alert or alarm is the risk of performing an unnecessary additional blood glucose test to confirm the erroneous sensor reading. The risk of medical harm may be mitigated through labeling which emphasizes that patients should confirm all CGM readings prior to making treatment decisions.
- 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. Risks of actions taken based on false negative hypoglycemic and hyperglycemic readings also include inappropriate administration of insulin or failure to administer or insufficient administration of extra carbohydrate which could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death.
- False positive hypoglycemic and hyperglycemic readings or alerts leading to unnecessary fingersticks to evaluate blood glucose, and disruption of user activity and sleep. If the false positive rate is too high it can result in 'alarm fatigue' and patients may deactivate the alerts/alarms
- Skin irritation or redness, inflammation, pain or discomfort, bruising, edema, rash, bleeding, infection, or allergic reaction due to either the sensor needle or the adhesive
- Sensor breakage leaving a sensor fragment under the skin

Risks of insulin pump include the following:

- Hypoglycemia from over-delivery of insulin due to a pump defect
- Hyperglycemia and ketosis possibly leading to ketoacidosis due to inappropriate pump failure or problems with the cannula, needle, or insulin infusion set tubing, resulting in cessation of or decreased insulin delivery
- Catheter dislodgement or fracture during infusion set insertion resulting in injury and/or inability to administer insulin

- Mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery
- Catheter occlusion resulting in missed insulin dosing
- Skin irritation, or redness, inflammation, pain or discomfort, bruising, edema, rash, bleeding, infection, or allergic reaction at the infusion site
- Failure of the infusion set or at the infusion site resulting in inability to administer insulin

Risks of the system include the following:

- Loss of communication between the pump and the sensor resulting in CGM values not being available to the user
- Use of inaccurate sensor values to make dosing decisions, resulting in an incorrect dose of insulin being delivered leading to hypo or hyperglycemia and their subsequent complications

These risks are similar to the risks associated with the separate components.

In conclusion, given the available information above, the data support that for the Paradigm REAL-Time Revel System the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The benefits of using the Paradigm REAL-Time Revel System with Enlite Sensor, as discussed above, outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on December 7, 2015.

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

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.