SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Continuous Glucose Monitoring (CGM) System
Device Trade Name:	iPro2 Continuous Glucose Monitoring (CGM) System
Device Procode:	MDS
Applicant's Name and Address:	Medtronic MiniMed 18000 Devonshire Street Northridge, CA 91325
Date(s) of Panel Recommendation:	None

Premarket Approval Application (PMA) Number: P150029

Date of FDA Notice of Approval: June 17, 2016

Priority Review: *Not Applicable*

II. INDICATIONS FOR USE

iPro2 CGM System (MMT-7745)

The iPro2 Recorder is to be used with either Enlite sensor or Sof-Sensor and is intended to continuously record interstitial glucose levels in persons with diabetes mellitus. This information is intended to supplement, not replace, blood glucose information obtained using a standard home glucose-monitoring device. The information collected by the iPro2 Recorder may be uploaded to a computer (with Internet access) and reviewed by healthcare professionals. This information may allow identification of patterns of glucose level excursions above or below the desired range, facilitating therapy adjustments which may minimize these excursions.

The iPro2 system:

- Is intended for prescription use only
- Does not allow data to be made available directly to patients in real time
- Provides data that will be available for review by physicians after the recording interval (up to 144 hours)
- Is intended for occasional rather than everyday use
- Is to be used only as a supplement, and not a replacement for, standard invasive measurement

Note:
The iPro2 recorder was approved for use with the Sof-Sensor under P980022/S071. P150029 is to support the new system including use of the iPro2 recorder with the Enlite sensor.

III. CONTRAINDICATIONS

None known.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the iPro2 CGM System labeling.

V. DEVICE DESCRIPTION

The iPro2 CGM System (MMT-7745) is comprised of a recorder which stores sensor glucose data, and a subcutaneously inserted glucose sensor. The iPro2 recorder was previously reviewed and approved for use in a system with a different sensor in P980022/S071 and has not been modified since the original approval. Additionally, the Enlite sensor was reviewed and approved in P120010 for use with the 530G System. Specifically, the following components are being approved for use together as a system:

iPro2 Digital Recorder (MMT-7741)
The iPro2 Recorder (MMT-7741) is a portable electrical current meter, data storage, and wired data communication system. The iPro2 Recorder functions as a "Holter-style" continuous glucose recorder for use under a physician's direction. The iPro2 Recorder is intended to measure, process, store, and upload glucose data from patients with diabetes mellitus. The device does not provide any real-time information, and data collected is intended only for retrospective review and analysis by a healthcare professional. The device is capable of measuring currents in the nanoamp range, filtering the measurements to reduce noise, encoding the measured current values, storing the values, and uploading the stored data via a wired communications link. Upload of data stored in the iPro2 Recorder is accomplished through placement of the iPro2 Recorder on the Docking Station (MMT-7742), which is connected to the PC using a USB cable.

Enlite Sensor (MMT-7008)
The Enlite Sensor is a single-use, disposable component, which is intended for use with the iPro2 Digital Recorder (MMT-7741) 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, 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 allows for safe disposal once the sensor is in place. The sensor base connects to the iPro2

Digital Recorder (MMT-7741) in order to permit continuous glucose recording. The Enlite Sensor is intended to be worn for up to six days.

Optional Accessory Devices
The following accessory devices are compatible with the iPro2 CGM system:

Device Name	**Model Number**
Docking Station	MMT-7742
Cleaning Plug	MMT-7744
USB Cable and AC Power Adapter	MMT-7747
Enlite Serter	MMT-7510
Additional Devices	
CareLink iPro Therapy Management Software for Diabetes	MMT-7340

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.

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.

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 iPro2 CGM system (model, MMT-7745) has been in commercial distribution in the United States since 2011 for use with the Sof-sensor (P980022). However, this system has not been previously available with the Enlite 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 530G system-P120010). The Enlite Sensor as a component of the MiniMed 530G system has been marketed in the European Union since 2011. These

devices have not been withdrawn from commercial distribution for any reason related to its safety and effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

Potential device-related, non-serious events related to CGM 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

Sensor breakage with fragments retained under the skin and catheter fracture during infusion set insertion are potential procedure-related complications. 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.

Information obtained from Medtronic MiniMed iPro2 CGM system may allow the healthcare provider to identify patterns of glucose level excursions above or below the desired range, and therefore can facilitate therapy adjustments which may minimize these excursions. The information collected is not intended to change patient management based on individual glucose values generated, but to guide future management of the patient based on response to trends noticed. Trends or patterns identified may be used to suggest when to take fingerstick measurements to better manage the patient. Inappropriate therapy changes based on the retrospective information provided by the Medtronic MiniMed iPro2 CGM system may result in deterioration of glycemic control if they occur.

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

Pre-clinical testing related to environmental exposure (including electromagnetic compatibility), biocompatibility, sterility, packaging/shelf life and shipping was performed on representative samples in support of the Enlite Sensor (model, MMT-7708) and the iPro2 Recorder (model, MMT-7741). See the SSED for P120010 for additional details on laboratory studies for the Enlite sensor, which are also

summarized below along with previous testing reviewed and approved for the iPro2 in P980022/S071, as well as additional testing to support this PMA.

I. Environmental Exposure

The following environmental exposure study (including electromagnetic compatibility) information was evaluated and approved as part of P120010 for the Enlite sensor and is applicable to this submission. Additionally, studies for the iPro2 recorder were evaluated and approved under P980022/S071. The following is an outline of studies performed:

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. All components tested demonstrated acceptable performance.

- 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

iPro2 Recorder
The iPro2 Recorder was subjected to Electromagnetic Compatibility testing to confirm that the device will function properly in the presence of electromagnetic signals that may be encountered in the intended use environment. The following testing was provided and demonstrated acceptable performance during the review of P980022/S071:

- Electro-Magnetic Immunity
- Conducted Emissions
- Radiated Emissions

- Electronic Article Surveillance Immunity
- Cell Phone Immunity
- Metal Detector Immunity
- Microwave Immunity
- Cordless Phone Immunity
- Wireless Network Immunity
- House Emitter & X-ray Immunity
- Electrostatic Discharge Susceptibility

Additional EMC testing was conducted for this PMA to support the use of the device in a home use environment. Specifically Magnetic Field Immunity testing demonstrated compliance with power-frequency magnetic field immunity of 30 A/m according to standard IEC 60601-1-2.

The following functional testing was conducted on the iPro2 recorder and provided to FDA for review in P980022/S071. Testing demonstrated acceptable performance

- Battery Life Test
- Chemical Resistance
- Storage Parameters
- Operating Parameters
- Steady State (Operating Humidity)

II. Mechanical Functionality

The following mechanical testing was conducted on the iPro2 recorder and submitted to the FDA for review in P980022/S071. Testing demonstrated acceptable performance.

- Mechanical Vibration Test
- Mechanical Drop Test
- Mechanical Shock Test
- Connector Cycling Test
- Push Test
- Molding Stress Relief
- Material Ingress

III. Biocompatibility Testing

The sponsor referenced biocompatibility testing from previously approved P120010 and P980022 for materials that consist of the iPro2 CGM system, including the 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 for the sensor was validated according to the requirements per ISO 11137 *Sterilization of Health Care Products-Radiation*. The remaining system component, the iPro2 recorder, is provided non-sterile; however, the device has validated cleaning/disinfection instructions (see labeling for the iPro2 CGM system for information on cleaning and disinfection).

V. Packaging/Shelf-Life:

The shelf-life of the Enlite Sensor (MMT7008) was validated to be up to six months when stored at +2°C to +30°C 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 (iPro2 recorder) were approved by FDA under P980022/S071. The iPro2 recorder can be used (cleaned and disinfected) up to 60 times and should be stored at -25 to +55°C.

VI. Software

The current software version for the iPro2 CGM system is v1.1A. Software verification and validation were carried out in accordance with the FDA guidance document *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices: General Principles of Software Validation: Final Guidance for Industry and FDA Staff (2002).* Software development activities included establishing detailed software requirements, linking requirements with associate verification tests, software code reviews, unit testing, system level testing and defect tracking and dispositioning to ensure the software conforms to patient needs and intended uses. Software was previously reviewed under P980022/S071.

VII. Human Factors Testing

The sponsor referenced human factors testing from previous submissions (P980022 and P120010) and provided new testing to support the proposed system configuration. New testing included the following:

- Evaluation of tasks regarding the removal of the iPro2 recorder from the Enlite sensor and inspection of fluids on the recorder before initiating contact with the iPro2 docking station.
- Evaluation of specific tasks performed in the software.

All testing demonstrated acceptable performance. 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.*

B. Animal Studies

None

C. Additional Studies

None

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The Enlite sensor was previously approved for use with the MiniLink transmitter as part of the 530G system (P120010). The MiniLink transmitter and iPro2 recorder have different signal processing algorithms, and due to these differences in the software and hardware architecture, the data processed by the iPro2 and the MiniLink may be different even if the same Enlite glucose sensor is used, and such differences might lead to additional glucose measurement bias. Therefore a re-analysis of the clinical data used to support approval of the Enlite sensor as part of P120010, was conducted. The analysis was used to determine the performance of the Enlite sensor with the signal processing algorithm used in the iPro2 recorder and establish a reasonable assurance of safety and effectiveness of the iPro2 System to continuously record interstitial glucose levels in persons with diabetes mellitus. A summary of this analysis is presented below.
The applicant conducted signal analysis testing to support the equivalence between data produced by the iPro2 recorder and the previously approved MiniLink transmitter.

During preliminary analyses the largest bias between the 530G-MiniLink and the iPro2 systems was observed when large rates of change in the signal occurred. The signal from these large rates of change corresponded with rapid changes in blood glucose levels that were physiologically unlikely to occur in subjects with diabetes. However, the overall data collected was sufficient to support acceptable performance of the iPro2 recorder output.

A. Study Design

For all information for the original clinical study where the sensor data was originally collected (including including inclusion/exclusion criteria and demographics) see the SSED for P120010.

Agreement of System Results with Reference Readings:

Agreement between the new System (re-analyzed data values) and blood glucose values was characterized using paired values between the new System and an established laboratory reference method (Yellow Springs Instruments Glucose analyzer) . 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 7272 for calibration 3-4 times per day and 7729 for calibration twice a day.

B. Safety and Effectiveness Results

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 a day)

Reference 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	7272	67.10%	78.60%	90.60%	96.40%	3.60%
<40*	3	66.70%	66.70%	66.70%	66.70%	33.30%
≥40-60*	604	64.60%	76.20%	88.60%	96.50%	3.50%
>60-80*	1369	56.80%	70.70%	86.40%	95.60%	4.40%
>80-180	3200	65.50%	77.20%	90.10%	95.70%	4.30%
>180-300	1613	76.40%	85.80%	94.40%	97.70%	2.30%
>300-350	313	79.90%	90.10%	98.10%	99.40%	0.60%
>350-400	143	83.20%	88.80%	93.00%	97.90%	2.10%
>400	27	55.60%	81.50%	88.90%	92.60%	7.40%

** For YSI 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)

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	7729	70.50%	81.70%	92.80%	96.70%	3.30%
<40*	3	66.70%	100.00%	100.00%	100.00 %	0.00%
≥40-60*	546	58.10%	75.80%	90.80%	95.20%	4.80%
>60-80*	1394	63.60%	75.50%	90.50%	95.30%	4.70%
>80-180	3280	68.10%	80.50%	92.70%	96.90%	3.10%
>180-300	1922	79.70%	87.20%	94.20%	97.00%	3.00%
>300-350	360	81.90%	90.60%	96.90%	99.40%	0.60%
>350-400	173	87.30%	91.90%	96.00%	98.80%	1.20%
>400	51	66.70%	88.20%	94.10%	96.10%	3.90%

** For YSI 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-YSI	Percent of YSI within 15/15% of CGM	Percent of YSI within 20/20% of CGM	Percent of YSI within 30/30% of CGM	Percent of YSI within 40/40% of CGM	Percent of YSI greater than 40/40% of CGM
Overall	7272	68.80%	79.80%	91.70%	97.00%	3.00%
≥40-60*	510	77.30%	87.10%	94.90%	97.60%	2.40%
>60-80*	892	79.40%	89.60%	96.50%	97.90%	2.10%
>80-180	3642	59.30%	71.40%	87.20%	95.70%	4.30%
>180-300	1734	77.20%	87.00%	96.00%	98.40%	1.60%
>300-350	298	84.20%	94.30%	98.70%	99.70%	0.30%
>350-400	196	77.60%	88.30%	98.00%	100.00 %	0.00%

** For CGM 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-YSI	Percent of YSI within 15/15% of CGM	Percent of YSI within 20/20% of CGM	Percent of YSI within 30/30% of CGM	Percent of YSI within 40/40% of CGM	Percent of YSI greater than 40/40% of CGM
Overall	7729	71.00%	82.30%	92.70%	96.90%	3.10%
≥40-60*	464	71.80%	83.40%	96.80%	98.50%	1.50%
>60-80*	983	80.20%	91.80%	98.30%	99.40%	0.60%
>80-180	3792	62.20%	74.80%	88.50%	95.30%	4.70%
>180-300	1904	79.80%	88.90%	95.70%	97.80%	2.20%
>300-350	345	85.80%	93.60%	97.70%	99.40%	0.60%
>350-400	241	79.30%	91.70%	97.50%	99.20%	0.80%

** For CGM 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 results in terms of absolute numbers and cumulative percentages for reference values less than the specified glucose levels (for 'LOW'), and for reference values greater than the specified 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	0	0	0	0	0	0
'HIGH'	Cumulative %	0%	0%	0%	0%	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	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	0	0	0	0	0	0
'HIGH'	Cumulative %	0%	0%	0%	0%	0%	

Concurrence of System and Laboratory Reference Values:
The percentage of concurring CGM readings and reference values are presented in Tables 4-A and 4-B, below. 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).

	Percent of Matched Pairs-in Each CGM Glucose Range for Each Ref Glucose Range											
	CGM (mg/dL)											
Ref (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%	66.7%	0.0%	33.3%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
>=40-60	604	0.0%	44.5%	38.6%	16.7%	0.2%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
>60-80	1369	0.0%	15.6%	39.3%	43.2%	1.8%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
>80-120	1412	0.0%	1.6%	7.8%	61.0%	28.2%	1.2%	0.2%	0.0%	0.0%	0.0%	0.0%
>120-160	1253	0.0%	0.0%	0.9%	9.6%	61.9%	25.1%	2.4%	0.1%	0.0%	0.0%	0.0%
>160-200	973	0.0%	0.0%	0.0%	1.7%	11.4%	60.1%	25.5%	1.0%	0.2%	0.0%	0.0%
>200-250	680	0.0%	0.3%	0.0%	1.2%	4.0%	16.6%	59.0%	17.4%	1.5%	0.1%	0.0%
>250-300	495	0.0%	0.0%	0.0%	0.6%	0.0%	2.0%	23.2%	53.9%	16.8%	3.4%	0.0%
>300-	313	0.0%	0.0%	0.0%	0.0%	0.0%	0.6%	2.6%	22.7%	47.3%	26.8%	0.0%

350												
>350-400	143	0.0%	0.0%	0.0%	0.0%	0.0%	2.1%	3.5%	7.0%	33.6%	53.8%	0.0%
>400	27	0.0%	0.0%	0.0%	0.0%	3.7%	0.0%	3.7%	3.7%	25.9%	63.0%	0.0%

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

	Percent of Matched Pairs-in Each CGM Glucose Range for Each Ref Glucose Range											
		CGM (mg/dL)										
Ref (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%	100.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
>=40-60	546	0.0%	39.6%	45.8%	13.7%	0.9%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
>60-80	1394	0.0%	16.5%	45.8%	35.4%	2.1%	0.3%	0.0%	0.0%	0.0%	0.0%	0.0%
>80-120	1327	0.0%	0.9%	7.0%	59.8%	31.2%	1.1%	0.1%	0.0%	0.0%	0.0%	0.0%
>120-160	1389	0.0%	0.0%	0.1%	13.4%	63.2%	22.1%	1.2%	0.0%	0.1%	0.0%	0.0%
>160-200	1045	0.0%	0.3%	0.0%	1.1%	18.7%	59.6%	19.3%	0.7%	0.1%	0.2%	0.0%
>200-250	857	0.0%	0.0%	0.1%	1.9%	4.7%	19.1%	58.1%	14.9%	1.1%	0.1%	0.0%
>250-300	584	0.0%	0.0%	0.0%	0.0%	0.9%	5.5%	18.0%	56.0%	17.3%	2.4%	0.0%
>300-350	360	0.0%	0.0%	0.0%	0.0%	0.0%	1.4%	3.9%	24.7%	48.6%	21.4%	0.0%
>350-400	173	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	2.9%	5.8%	30.1%	61.3%	0.0%
>400	51	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	3.9%	3.9%	11.8%	80.4%	0.0%

Additional Evaluation of Agreement:

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, 3.37% lower than the reference (Mean relative difference) and with an average 14.28% 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, 1.76% lower (Mean relative difference) than the reference and with an average 13.62% 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-YSI	Mean percent difference (%)	Median percent difference (%)	Mean absolute percent difference (%)	Median absolute percent difference (%)
Overall	7272	-3.37	-4.94	14.28	10.65
40-60*	510	9.82	8.50	11.35	9.38
61-80*	892	-1.89	-3.95	10.63	8.95
81-180	3642	-7.27	-7.74	15.30	11.81
181-300	1734	-2.46	-3.25	10.49	8.20
301-350	298	-2.31	-1.58	8.46	7.02
351-400	196	-7.69	-8.25	10.61	9.15

** For CGM range ≤ 80 mg/dL, the differences in mg/dL are included instead of percent 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-YSI	Mean percent difference (%)	Median percent difference (%)	Mean absolute percent difference (%)	Median absolute percent difference (%)
Overall	7729	-1.76	-3.69	13.62	9.86
40-60*	464	10.66	9.95	12.18	10.07
61-80*	983	-4.08	-5.25	9.49	7.85
81-180	3792	-4.40	-6.05	14.86	11.31
181-300	1904	-0.41	-1.88	9.90	7.28
301-350	345	-1.59	-1.30	8.48	6.61
351-400	241	-4.37	-3.61	8.94	6.62

** For CGM range ≤ 80 mg/dL, the differences in mg/dL are included instead of percent 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 5.19% higher than the reference blood glucose values and that half of the time the System read less than 11.11% different than reference blood glucose values for calibration three to four times per day. For calibration twice a day, the System read less than 3.83% higher than the reference blood glucose values and that half of the time the System read less than 10.15% 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)

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	7272	7.40	5.19	15.57	11.11
<40*	3	23.52	10.65	23.52	10.65
40-60*	604	9.55	8.82	13.97	11.05
61-80*	1369	10.07	9.85	15.94	12.75
81-180	3200	7.04	6.12	13.57	10.08
181-300	1613	0.77	1.12	10.79	7.90
301-350	313	0.58	0.31	9.30	7.97
351-400	143	-5.81	-3.24	9.57	6.41
>400	27	-16.04	-14.03	16.04	14.03

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

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

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	7729	5.47	3.83	14.44	10.15
<40*	3	10.52	11.90	10.52	11.90
40-60*	546	10.97	9.93	14.96	12.28
61-80*	1394	8.34	7.15	14.40	11.12
81-180	3280	5.71	5.25	12.76	9.87
181-300	1922	-1.24	0.00	10.40	7.43
301-350	360	-1.91	-1.56	9.06	6.58
351-400	173	-4.50	-1.92	8.25	6.18
>400	51	-12.71	-11.60	12.71	11.60

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

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

YSI Glucose Ranges (mg/dL)	Number of paired CGM-YSI values	Percent of CGM values within 15 mg/dL/15% of YSI	Percent of CGM values within 20 mg/dL/20% of YSI	Percent of CGM values within 30 mg/dL/30% of YSI	Percent of CGM values within 40 mg/dL/40% of YSI	Percent of CGM values greater than 40 mg/dL/40% of YSI
Overall	150001	68.90%	80.20%	91.70%	96.50%	3.50%
0-2 hours	7010	70.40%	81.10%	92.20%	96.90%	3.10%
2-4 hours	5320	69.20%	80.50%	91.60%	96.40%	3.60%
4-6 hours	2153	64.90%	77.60%	90.60%	95.90%	4.10%
6-8 hours	363	59.50%	73.60%	89.50%	93.10%	6.90%
8-10 hours	106	67.00%	81.10%	96.20%	99.10%	0.90%
10-12 hours	33	81.80%	90.90%	97.00%	97.00%	3.00%
Beyond 12 hours	4	50.00%	100.00%	100.00%	100.00%	0.00%
Before Calibration	12	50.00%	66.70%	83.30%	100.00%	0.00%

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 iPro2 recorder is based on the pre-clinical bench testing results and re-analysis of clinical data as discussed above. The following tests were performed to determine the effectiveness of the device: environmental exposure, functional testing, electro-magnetic compatibility (EMC), biocompatibility, cleaning/disinfection, packaging/shelf-life, software verification and validation, and human factors/usability. Bench testing data provided was previously approved and confirmed system capability of sensing, storing, and uploading data. The above clinical data supports that the iPro2 with Enlite sensor performs adequately to be effective for its intended use. Acceptable agreement was observed; please see tables in Section X above.

B. Safety Conclusions

Evaluation of the risks of the device are based on post-market data (MDR analysis) and non-clinical data in Sections IX, above. Adverse events related to treatment decisions which lead to hypoglycemia or hyperglycemia are unlikely to occur with the iPro2 system, as the glucose values recorded by the system are masked to the user; therefore, the user cannot make treatment decisions based on these values in real time.

Potential device-related, non-serious events related to CGM 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

Sensor breakage with fragments retained under the skin and catheter fracture during infusion set insertion are potential procedure-related complications. 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.

Information obtained from Medtronic MiniMed iPro2 CGM system may allow the healthcare provider to identify patterns of glucose level excursions above or below the desired range, and therefore can facilitate therapy adjustments which may minimize these excursions. The information collected is not intended to change patient management based on numbers generated but to guide future management of the patient based on response to trends noticed. Trends or patterns identified may be used to suggest when to take fingerstick measurements to better manage the patient. Inappropriate therapy changes based on the retrospective information provided by the Medtronic MiniMed iPro2 CGM system may result in deterioration of glycemic control if they occur. However, the healthcare providers' training and clinical judgment would reduce the likelihood of acute or long-term adverse effects of inappropriate treatment due to inaccurate results.

C. Benefit-Risk Conclusions

Summary of Benefits:

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

The iPro2 with Enlite sensor is intended to supplement self-monitoring of blood glucose to retrospectively track and trend interstitial glucose levels as estimates of glucose excursions in the blood.

These functions are not feasible using traditional blood glucose monitoring as blood glucose meters only provide information about discrete, intermittent blood glucose levels and therefore are unable to provide information regarding patterns of glycemic excursions throughout the day and night when patients may be unable to test their

blood glucose. The CGM can evaluate glucose trends over several days to detect patterns which may indicate a need to adjust therapy, but might be missed with infrequent, intermittent blood glucose monitoring. Therefore, this device provides benefit to users not possible with traditional glucose monitoring.

The CGM component of the device 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/S071). The Enlite sensor has an extended wear period relative to the Sof-Sensor (6 days vs. 3 days). The iPro2 with Enlite sensor 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.

In summary, benefits of the CGM component of the system include:

- Providing information regarding patterns of glycemic excursions throughout the day and night when patients may be unable to test their blood glucose
- Aiding in the prevention of extremes of glycemia.
- Providing 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.
- Extending sensor wear period relative to previously approved version of the device.

Summary of Risks:

Risks of the CGM and sensor:

- Sensor error resulting in incorrect glucose readings. There is a risk of deterioration of glycemic control if treatment changes are made based on the retrospective analysis of incorrect glucose readings.
- 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

Summary of other factors:

Patient Perspectives
Patient perspectives considered during the review included:
Patients want a variety of devices that provide information regarding their glucose control to inform decision making with their health care providers on lifestyle changes and treatment decisions. This information was gathered during patient oriented conferences and face-to-face meetings with patients.

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 iPro2 CGM system, as discussed above, outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on June 17, 2016.

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.