SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Continuous Glucose Monitoring System
Device Trade Name:	Dexcom G4 PLATINUM Continuous Glucose Monitoring System
Device Procode:	MDS
Applicant's Name and Address:	Dexcom, Inc. 6340 Sequence Drive San Diego, CA 92121
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P120005
Date of FDA Notice of Approval:	October 5, 2012
Expedited:	not applicable

II. INDICATIONS FOR USE

The Dexcom G4 PLATINUM Continuous Glucose Monitoring System is a glucose monitoring device indicated for detecting trends and tracking patterns in persons (age 18 and older) with diabetes. The system is intended for single patient use and requires a prescription.

The Dexcom G4 PLATINUM System is indicated for use as an adjunctive device to complement, not replace, information obtained from standard home glucose monitoring devices.

The Dexcom G4 PLATINUM System aids in the detection of episodes of hyperglycemia and hypoglycemia, facilitating both acute and long-term therapy adjustments, which may minimize these excursions. Interpretation of the Dexcom G4 PLATINUM System results should be based on the trends and patterns seen with several sequential readings over time.

III. CONTRAINDICATIONS

- Remove the Dexcom G4 PLATINUM sensor, transmitter, and receiver before Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, or

diathermy treatment. The Dexcom G4 PLATINUM System has not been tested during MRI or CT scans or with diathermy treatment. The magnetic fields and heat could damage the device so that it might not display sensor glucose readings or provide alerts, and you might miss a low or high blood glucose value.

- Taking medications with acetaminophen (such as Tylenol) while wearing the sensor may falsely raise your sensor glucose readings. The level of inaccuracy depends on the amount of acetaminophen active in your body and may be different for each person.

IV. WARNINGS AND PRECAUTIONS

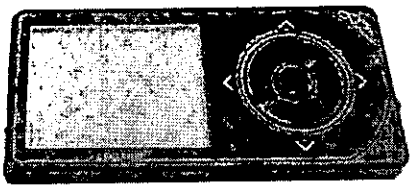
The warnings and precautions can be found in the Dexcom G4 PLATINUM Continuous Glucose Monitoring System labeling.

V. DEVICE DESCRIPTION

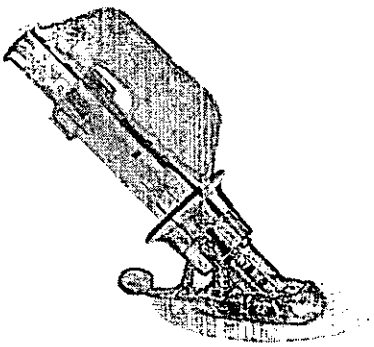
The Dexcom G4 PLATINUM Continuous Glucose Monitoring System ("The System") is a glucose monitoring device indicated for detecting trends and tracking patterns in persons (age 18 and older) with diabetes. The System is designed to provide continuous measurements of interstitial fluid glucose over the measuring range of 40 to 400 mg/dL for up to seven days of use. The claimed insertion site for the sensor is the abdomen.

Once the sensor is inserted under the skin of the abdomen and attached to the transmitter, the System requires a start-up period prior to the initial calibration. The start-up period, the time required for the Sensor to equilibrate, requires a minimum of two hour from Sensor insertion. At the end of this period, the system prompts the user to calibrate the device with fingerstick blood glucose measurements using any FDA-cleared home blood glucose meter. The user then manually enters the blood glucose values using a menu-driven interface on the device. After calibration, the System provides a glucose reading once every 5 minutes as well as trend graphs which are updated periodically. The System also has programmable High and Low Glucose Alerts and a non-changeable Low Glucose Alarm set at 55 mg/dL.

The System consists of the following components: Sensor, Transmitter, and Receiver:



Dexcom G4 PLATINUM
Receiver



Dexcom G4
PLATINUM Sensor

Dexcom G4 PLATINUM
Transmitter

A. Dexcom G4 PLATINUM Sensor

The G4 PLATINUM Sensor (the Sensor) is comprised of a sensor applicator, an adhesive pad, transmitter mount and the sensor probe. The sensor can be worn for up to 7 days. The Sensor is a sterile device inserted by the user into the abdominal subcutaneous tissue using the applicator. The applicator is adhered to the surface of the skin with a standard medical grade adhesive pad. The applicator contains a 26-gauge introducer needle that contains the sensor probe. The needle is not exposed, or even visible, to the user during the insertion process. After deployment of the introducer needle, the needle is retracted back into the applicator. The sensor probe remains beneath the surface of the skin and uses the enzyme glucose oxidase to convert the glucose in the interstitial fluid around the sensor into an electrical current proportional to the ambient glucose concentration.

The applicator is detached and disposed by the user, exposing a transmitter mount ready for placement of the transmitter.

B. Dexcom G4 PLATINUM Transmitter

The G4 PLATINUM Transmitter (the Transmitter) is a miniature radio transmitter operating at an internationally-accepted radiofrequency. After sensor insertion and removal of the applicator, the user manually places the Transmitter into the transmitter mount on the adhesive pad already attached to the skin. The Transmitter contains all the electrical circuitry necessary for the operation of the electrochemical sensor and also all the radiofrequency circuitry necessary to transmit the Sensor signal to the Receiver. The Transmitter collects the small electrical current from the

Sensor and transmits the Sensor signal wirelessly to the Receiver at regular 5-minute intervals. The Transmitter is reusable and can be used for repeated 7-day sessions by a single-user over the lifetime of the battery encased in the device.

C. Dexcom G4 PLATINUM Receiver

The G4 Receiver (the Receiver) is a small hand-held device that contains an antenna and the associated electrical circuitry to receive the wireless sensor signal from the transmitter. The Receiver contains a rechargeable battery. In typical use, the Receiver may last for up to 3 days before requiring recharging. The user must maintain the Receiver within 20 feet or less of the Transmitter, which is attached to the sensor on the body. The Receiver also contains calibration and signal processing algorithms required to convert the sensor electrical signal to glucose values in mg/dL that can be displayed to the user. Calibrations are performed twice daily by the patient using measurements from standard commercially-available FDA-cleared blood glucose meter devices and manually entered into the Receiver through a simple data entry menu. After calibrating the system, the Receiver automatically displays the current glucose value, trend graphs of recent glucose values and rate of change arrows once every five minutes. The Receiver provides audible or vibratory alerts for high and low glucose values.

The configurable Receiver High and Low Glucose Alerts can be set by the user in consultation with their health care provider to provide warning when their current glucose level is outside of their target range. Dashed lines on the Receiver screen indicate the current alert level settings. The user can configure the Receiver to provide audible, vibratory or combined audible and vibratory alerts. The Receiver also contains a non-configurable low glucose alarm at 55 mg/dL to provide users additional warning of hypoglycemia.

The Receiver contains a mini-USB port for uploading Sensor data to a personal computer. Dexcom Studio software is an optional accessory data management program intended to allow the transfer of glucose data stored by the Receiver to a personal computer (PC). This software can be used to view trends, track patterns and create custom charts to display glucose trends by either clinicians or the user. The software is available for users to download from the Sponsor's website.

Please refer to the Dexcom G4 Platinum User's Guide for more detail.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Control of diabetes can be achieved through a combination of methods and behaviors. Self behaviors include healthy eating, taking medications, as appropriate, and being active. Methods of controlling glucose levels (glycemic control) have been shown to reduce severe diabetes-related complications. Methods of monitoring glycemic control include periodic measurement of Hemoglobin A1c (HbA1c), which reflects average

blood glucose levels over a three month period. Self-monitoring of blood glucose using glucose meters and test strips provides quantitative measurements of fingerstick blood glucose at a single point in time for patients and their healthcare providers to monitor the effectiveness of glycemic control and make more immediate treatment modifications.

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

There are similar CGM systems currently on the market from this sponsor and other sponsors.

VII. MARKETING HISTORY

The Dexcom G4 PLATINUM Continuous Glucose Monitoring System has not been marketed in the United States but received a CE mark and was commercialized in the European Economic Community in July 2012. The device has not been withdrawn from marketing for any reason related to its safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

The following events are possible adverse device effects of inserting a Sensor and wearing the adhesive patch: local infection, inflammation, pain or discomfort, bleeding at the glucose Sensor insertion site, bruising, itching, scarring or skin discoloration, hematoma, tape irritation, Sensor or needle fracture during insertion, wear or removal.

There are potential risks due to missed alerts, false alerts, false negative hypoglycemia and hyperglycemic readings and false positive hypoglycemia and hyperglycemia readings by the device. There are additonal possibible risks if the system inaccurately calculates the rate of change of glucose.

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

IX. SUMMARY OF PRECLINICAL STUDIES

A summary of the non-clinical laboratory studies that were performed on the G4 Platinum CGM System are summarized below and in Tables 1-2:

A. Laboratory Studies

Bench Performance Testing: Pre-clinical testing was performed on the Sensor, Transmitter and Receiver. This testing involved Environmental and safety testing and physical and mechanical testing (e.g. mechanical vibration, mechanical drop,

temperature shock, temperature and humidity exposure, atmospheric pressure, needle insertion force, needle bond strength, and needle resistance to fracture), This testing is summarized in the Tables below (Tables 1A-1C):

Table 1A – Sensor Testing

Test Description	Test Purpose	Acceptance Criteria	Device Configuration	Test Results
Sensor Retention	Demonstrate that the minimum force required to retain the sensor meets product specification	≥0.04 lbs	G4 Sensor Assembly; G4 Transmitter	PASS
Safety Card Removal	Demonstrate that the force required to remove the safety card meets product specification	≤ 3 lbs	G4 Sensor Assembly	PASS
Needle to remain in applicator after deployment	Demonstrate that the force required to cause failure of the cannula carrier At least 1.0 lb force (lower limit) snaps meets product specifications	At least 1.0 lb force (lower limit)	G4 Applicator	PASS
Sensor Resistance to Fracture Under Repetitive Bending	Demonstrate that a G4 Sensor has improved resistance to fracture under repetitive bending when compared to the existing SEVEN PLUS product	Minimum 2x increase in cycles to wire failure at 0.032" bend radius compared to SEVEN PLUS	G4 Sensor; SEVEN PLUS Sensors	PASS
Needle Bond Strength	Demonstrate that the force required to pull the needle to failure meets product specification	At least 2.0 lb force (lower limit)	G4 Sensor and Applicator	PASS
Push Rod Bond Strength	Demonstrate that the force required to pull the push rod to failure meets product specification	At least 1.0 lb force (lower limit)	G4 Sensor and Applicator	PASS
Cannula Bond Strength	Demonstrate that the force required to pull the cannula to failure meets product specification	At least 6.5 lb force (lower limit)	G4 Sensor and Applicator	PASS
Deployment	Demonstrate that the plunger, cannula carrier, pushrod, needle carrier, and safety locks deploy correctly	Plunger, needle, cannula, pushrod, and safety locks operate correctly	G4 Sensor and Applicator	PASS
Sensor Angle Measurement	Demonstrate that the angle of the sensor meets product specification	45°±5°	G4 Sensor and Applicator	PASS
Sensor Deployment Depth	Demonstrate that the depth of the Sensor below the adhesive pad meets product specification	Distal tip of the Sensor to be between 0.35" (lower limit) and 0.55" (upper limit)	G4 Sensor and Applicator	PASS

Humidity Resistance	Demonstrate that the resistance to humidity meets product specification	Counts ≤6000 (187.5 pA)	G4 Transmitter; Sterilized G4 Sensor Assembly; G4 Receiver	PASS
Adhesive/ Base Peel Test	Demonstrate that the pad exhibits some cohesive failure such as pad ripping following a base peel test, as per product specification	Pad must display some cohesive failure	G4 Applicator	PASS
Water Resistance	Demonstrate that the product meets the requirement for water resistance	Counts ≤6000 (187.5 pA)	Sterilized G4 Sensor Assembly; ;Transmitter; G4 Receiver	PASS
Reference Electrode Capacity	Demonstrate that the reference capacity of the G4 Sensors is sufficient to meet the intended use of 7 days of use	≤10.0% MARD after 7 days	G4 Sensors	PASS
Needle Insertion Force	Demonstrate that the force required to insert a needle through a chamois meets product specification	Not to exceed 5 lb force (upper limit)	G4 Applicator	PASS
Cannula Withdrawal Force	Demonstrate that the force required to withdraw the cannula meets product specification	Not to exceed 7.5 lb force (upper limit)	G4 Applicator	PASS
Bail Snap Out Force	Demonstrate that the force required to remove the bail from the device meets product specification	≤2.8 lbs	G4 Sensor Assembly	PASS
Bail Insertion Cycles	Demonstrate that the bail is capable of 3 insertion cycles	Bail to insert transmitter into sensor base 3 times with bail not falling out	G4 Sensor Assembly; G4 Transmitter	PASS
Applicator Body Release from Base	Demonstrate that the Applicator Body is easily removable from Sensor Base	Applicator can be easily released from base	G4 Sensor and Applicator	PASS
Contact Resistance	Demonstrate that the transmitter meets the product specification for Sensor contact resistance	Contact Resistance ≤5 MΩ	G4 transmitter, Sterilized G4 Sensor Assembly, and G4 Receiver	PASS

Contact Resistance Change	Demonstrate that the transmitter meets the product specification for Sensor contact resistance change	Contact Resistance change ≤5 MΩ	G4 transmitter, Sterilized G4 Sensor Assembly, and G4 Receiver	PASS

Table 1B – Transmitter Testing

Test Description	Test Purpose	Acceptance Criteria	Device Configuration	Test Results
Operating Temperature Validation	Validate the reliable operation of the G4 Transmitter across its specified temperature range.	Each temperature test shows no less than 44 out of 45 consecutive packets are successfully transmitted by each unit under test. A packet transmission is considered successful if it has a clear status and a raw count value between 42,665 and 49,765 counts.	G4 Transmitter Assemblies	PASS
Humidity, Atmospheric Pressure, and Vibration Tests	Demonstrate product conformance to humidity, pressure and vibration specifications Humidity: 10- 95%, non-condensing Pressure: 7.5± 0.5 psi to 15±1.1 psi Vibration resistance: ASD spectrum level: 0.1 G2/Hz 5-150 Hz, 3 axes, 30 minutes per axis	Humidity and Pressure Tests Tested as variable data: 15 samples tested, with 0 failures, that must satisfy applicable tolerance limits when evaluated using the tolerance limit equations $M + k*s \leq U$. Vibration Test Tested as attribute data: All 30 samples must pass, 0 failures in order to meet Confidence Level of 95% and Reliability of 90%.	G4 Transmitters; G4 Sensor Assemblies; G4 Receivers	PASS
Drop Resistance	Demonstrate product conformance to drop resistance specifications	The raw count reading after the drop test is within ±10% of the initial reading. The Transmitter can be held in a Sensor	G4 Transmitters	PASS

		base and there are no added scratches or defects within the Transmitter seal area.		
Water Resistance	Demonstrate product conformance to water resistance specifications (IP28)	Acceptance criteria as detailed in EN 60601-1-11:2010	G4 transmitters	PASS

Table 1C – Receiver Testing

Test Description	Test Purpose	Acceptance Criteria	Device Configuration	Test Results
Operating/ Storage Temperature (not charging and relative humidity uncontrolled – ambient RH < 85%)	Demonstrate reliable operation of the G4 Receivers across Specified temperature	All units must demonstrate functionality with audio alarm, vibrator alarm, and transmission receipt. All units must pass the final functional testing process and all units must receive a minimum of 95% packets during testing period.	G4 Receivers; G4 Transmitters	PASS
Operating Storage Humidity	Demonstrate reliable operation of the G4 Receivers across its specified humidity range of 10-95%.	All units must demonstrate functionality with audio alarm, vibrator alarm, and transmission receipt. All units must pass the final functional testing process and all units must receive a minimum of 95% packets during testing period.	G4 Receivers; G4 Transmitters	PASS
Operating Storage Pressure (temperature and humidity uncontrolled ambient: 20°C-5°C and relative humidity	Operating/Storage Pressure (temperature and humidity uncontrolled ambient: 20°C-5°C and relative humidity between 20% and 90%)	All units must demonstrate functionality with audio alarm, vibrator alarm, and transmission receipt. All units must pass the final functional testing process and all units must receive	G4 Receivers: G4 Transmitters	PASS

between 20% and 90%)		a minimum of 95% packets during testing period.		
Drop Resistance	Verify compliance to the product requirement regarding drop resistance with and without the carrying case	All units must pass the final functional test and have no signs of a hazardous condition.	G4 Receiver; G4 Receiver carrying case	PASS
Ingress Protection	Demonstrate that the G4 Receiver (with USB door closed) is protected against 15 degree dripping and 12.5 mm object access (IP22)	Receiver must meet acceptance criteria per applicable standard, IEC 60601-1-11 G4 Receiver with USB access door closed.	G4 Receiver	PASS
Battery Verification	Demonstrate product conformance to the general performance of the battery, including battery charging ability at temperature, ability to retain time with the backup battery, accuracy of the battery gauge, confirmation of power on ability following battery discharge, and charge times using a wall charger and powered USB port.	Operational Temperature While Charging: All units must fully charge to 100% at 40°C. Time Retention: All units must retain time for a minimum of 3 days while in Shutdown. Battery Gauge: accuracy within ±25% Power On: All units must Power On when connected to a charger after the battery has been depleted. Wall Charger Charge Time: fully charged after 3 hours Power USB Port Charge Time: fully charged after 5 hours	G4 Receivers; G4 Receiver Wall Charger; G4 Receiver USBCable	PASS

Biocompatibility: Biocompatibility testing was performed on the sterile components of the System, including the Sensor Applicator, Sensor Probe, and Sensor pod as well as the Transmitter. Biocompatibility testing was conducted in accordance with ISO 10993-1. The following table (Table 2) includes a description of the testing performed and the results.

Table 2. G4 Platinum System Biocompatibility Results

Test	Result
Cytotoxicity (MEM Elution)	Non-toxic
Sensitization	No evidence of sensitization
Intracutaneous Reactivity	Non-irritant
Acute Systemic Toxicity (Acute Systemic Injection Test)	Non-toxic
Systemic Toxicity (Material Mediated Pyrogen)	Non-pyrogenic
Subchronic Toxicity (30 day)	Non-toxic
Genotoxicity (Ames Test)	Non-mutagenic
Genotoxicity (Chromosome Aberration)	Non-genotoxic
Genotoxicity (Mouse Micronucleus)	Non-mutagenic
Muscle Implantation	Non-irritant

Sterility Assurance: Sterilization of the System components (applicator, transmitter housing/base, insertion needle, Sensor) utilized electron beam radiation using the VD_{max}^{25} method. The minimum exposure dose required to sterilize the product with a sterility assurance level of 10-6 is 25.0 kGy. Transmitters and Receivers are not sterile products.

To validate the sterilization process, the procedure for method VD_{max}^{25} for multiple production batches outlined in ANSI/AAMI/ISO 11137-2:2006 was followed. In order to determine the sterilization dose, a bioburden recovery method test was initially performed, followed by the determination of the bioburden recovery factor. The average bioburden was determined for three production lots. The total overall average bioburden was then calculated using the recovery factor and was used to obtain the VD_{max}^{25} dose. A verification dose experiment was then performed using 10

samples from one production lot. Each sample was individually subjected to a test of sterility. Since there was no more than one positive test of sterility from the 10 tests carried out, 25 kGy was substantiated as the minimum sterilization dose. Dose mapping was also performed at 25 kGy using the final product packaging to confirm proper irradiation.

Electromagnetic Compatibility and Interference: Acceptable electromagnetic compatibility (EMC) and electromagnetic immunity (EMI) testing was performed for the G4 Platinum Transmitter and G4 Platinum Receiver. Criteria used in the testing included the following occurrences that were correlated to the disturbance: device turning on or off, changing modes, resetting, no longer functioning, the device becoming unreadable for more than 5 seconds, the device changing settings, alarm failures, power supply ceases to source +5VDC4 for more than 5 seconds, packets are dropped at a rate of no more than 1 out of 205 consecutive transmissions (95% success), EGV Value is outside of the +/- 5mg/dL or +/- 5% (whichever is greater) of the starting baseline value for more than one consecutive packet (radiated RF immunity testing only), Receiver database is erased, Receiver date or time is changed (other than normal time progression), Transmitter ID is changed (in receiver), Low Glucose Alarm ceases to annunciate, the raw count during manufacturing test mode deviates more than +/- 5% of the baseline counts (radiated RF immunity testing only), the system fails the functional test after EMC testing.

Radiofrequency (RF) communication testing was performed demonstrating compliance with Federal Communications Commission standards (Title 47 Part 15). Radiated Emissions Test, Occupied Bandwidth, and Band-edge Measurement testing was performed.

Radiofrequency wireless testing, including wireless co-existence, was conducted on the System. Testing indicated that the System can operate in the presence of RF interference and co-exists with other wireless devices operating in the same vicinity. Other wireless testing successfully verified the performance of the RF transmission intervals, RF frequency intervals, RF carrier frequency, and listen before talk testing. The communication distance of 20 feet was verified and successful RF communication occurred when worn in different locations and orientations on a human torso model.

Shelf-life and Storage Stability: Real-time studies were conducted to examine the effect of aging on the sterilized Sensors and to determine an appropriate shelf life for sensors stored at ambient conditions. The in-vitro Sensor performance and product functionality data collected from this study was used in the determination of appropriate shelf-life for Sensors and applicators. Testing included: deployment testing, seal integrity testing, contact resistance testing, reference electrode capacity testing, Sensor pouch seal strength test, Sensor pouch bubble leak test, shelf-life sensor performance. Shelf-life testing was provided to support the 6 month Sensor shelf-life. The labeling instructs the user to store the Sensors at 36°F to 77°F and

between 15% and 85% relative humidity and indicates that the Sensors should not be stored in the freezer.

Adequate testing was performed to support a shelf-life for the Transmitter battery (which translates to the Transmitter shelf-life) of 8 months and a normal operating battery/Transmitter life of 6 months. The Transmitters and Receivers should be stored at 32°F to 113°F, between 15% and 85% relative humidity.

Packaging Integrity/Shipping Testing: The packaging consists of a Receiver kit, a Transmitter kit, and a Sensor kit that may contain a single Sensor or a 4-pack. The units are placed in a box for shipment in the US. Testing was performed per ISTA 2A 2008 guidelines using samples with representative shipping configurations comprised of the Sensor, Transmitter, and Receiver kits. The packaged samples were subjected to atmospheric conditioning, vibration, compression and drop tests and the structural integrity of the packaging, and pouch seal examined. The individual components, i.e., Sensor, Transmitter, and Receiver met the functional performance requirements per protocol at 95% confidence/90% Reliability. The results passed demonstrating that the G4 Platinum System packaging met the applicable requirements per product specifications.

The microbial barrier properties of the material used in the manufacture of the sterile Sensor pouch was evaluated according to ASTM F1608. Results demonstrated that the material met the applicable requirements per product specifications.

Software Validation: Testing was performed to ensure the performance of each of the manufactured devices has met the software design specification and software requirements specifications established for each item. The verification and validation activities are completed according to the FDA guidance entitled General Principles of Software Validation: Final Guidance for Industry and FDA Staff released January 11, 2002.

Software validation was provided for the software programs for the Receiver, the Transmitter, and the Studio Software (the program to allow the user or healthcare provider to download results from the Receiver to a PC to view the data and trends).

Verification and validation of the software implementation was accomplished through software code reviews, unit testing, and integration testing. These evaluations verify that the software implementation satisfies the design implementation as defined in the Software Requirements Specifications and validate that the software conforms to user needs and intended uses.

Human Factors and Usability Testing: Usability testing (user-interface design validation) of the System was performed following the Draft Guidance for Industry and FDA staff titled, *Applying Human Factors and Usability Engineering to Optimize Medical Device Design*, dated June 22, 2011. The testing considered device users, use environment, and user interfaces including device labeling and

training. The summative study involved simulated use of the CGM system with 30 participants with differing levels of CGM experience and diabetes therapy that were presented with a series of realistic CGM use scenarios and asked for their response. The study was intended to collect both observational and qualitative data. It was also designed to assess the adequacy of the user instructions and training materials to support safe and effective use of the device.

B. Animal Studies

No animal studies were conducted using the Dexcom G4 Platinum CGM System.

C. Additional Studies

None

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a pivotal clinical study to establish a reasonable assurance of safety and effectiveness with the Dexcom G4 Platinum System for detecting trends and tracking patterns when used as an adjuvant to blood glucose testing in subjects with diabetes mellitus. This study was performed in the US under IDE #G110107/S001. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Subjects were enrolled between December 9, 2011 and February 10, 2012. The database for this PMA reflected data collected through February 10, 2012 and included enrolling 72 patients. There were 4 investigational sites.

The purpose of the pivotal study was to evaluate the safety and effectiveness of the G4 Platinum System when used as an adjuvant to blood glucose testing over a 7-day period in subjects >18 years-old with diabetes mellitus. The study was an open-label, non-randomized, single-arm, multi-center, pivotal study.

The 72 enrolled subjects wore the G4 Sensor for one week (168 hours) and participated in both an in-clinic and a home use portion of the study. Subjects were instructed to use CGM information as an adjunct to (not a replacement for) using standard self-monitoring blood glucose (SMBG) meters for the self-management of diabetes. After being provided instructional materials, subjects inserted the sensor themselves.

One hundred and eight (108) Transmitters and 108 Receivers were used with no replacements needed. One hundred twenty-one (121) Sensors were inserted, 13 (11%) of which were replacements. Sensors were replaced primarily due to mechanical failures (e.g. sensor wire not attached to pod or sensor attached to adhesive) or user errors (e.g. improper insertion technique).

In-Clinic Portion of the Study –
The primary objective was to characterize the System performance with respect to laboratory reference measurements on venous blood samples for all study subjects (there was no separate control group). The device performance was primarily evaluated in terms of point and rate accuracy of the System in comparison to a clinical laboratory reference method, the Yellow Springs Instrument 2300 STAT Plus Glucose Analyzer (YSI). The evaluation of safety and effectiveness involved the assessment of many analyses of the data generated during the study (see Tables 5 to 17; Section X.D.2); however, the criteria used by the sponsor to assess point accuracy was the proportion of System readings that were within ±20% of the YSI reference value for glucose levels >80 mg/dL and within ±20 mg/dL for YSI glucose levels <80 mg/dL. The trend accuracy of the device performance was evaluated, as well as the temporal System accuracy at different glucose rates of change and different glucose ranges (hypoglycemic, euglycemic, and hyperglycemic ranges).

The performance of the System was determined across the 7 days of wear time. All subjects were asked to come into the clinic on Day 1, 4, and 7 for a 12-13 hour in-clinic session. To obtain primary matched paired measurements subjects had venous blood drawn from an intravenous catheter approximately once every 15 +/- 5 minutes to allow for frequent comparison of the System to YSI. The YSI measurements were made on plasma samples obtained from the collected venous samples. Readings from the System were reported every 5 minutes and paired with YSI values in order to characterize the agreement between the System and YSI.

During the in-clinic sessions the study investigators were blinded to the G4 sensor results and all treatment decisions were based on the reference glucose readings (YSI). All subjects were also asked to take two fingerstick measurements per hour using the provided SMBG meter (LifeScan OneTouch Ultra2) and additionally as indicated for diabetes management or clinical safety purposes.

During the in-clinic portion of the study the glucose levels of certain subjects were deliberately manipulated (with close observation by the study investigator staff) to induce high or low blood glucose via carbohydrate consumption, insulin dosing, and exercise to achieve YSI sample measurements within target glucose bins following a protocol specific guideline. This manipulation was included in the study design to allow the collection of comparison data at glucose concentrations that spanned the claimed measuring range of the System (40-400 mg/dL).

Sensors were calibrated approximately once every 12 hours, using the SMBG meter values obtained from the LifeScan OneTouch Ultra2 meter. Throughout the 7-day wear period, the Sensor was calibrated with an average of 2 fingersticks per day (approximately once every 12 hours).

Precision of the System was assessed on a subset of patients (36 subjects from two of the clinical sites) wearing two Systems simultaneously. One of each of the paired systems was blinded (CGM values, trends, alerts/alarms not provided) and the other was unblinded during home use. Subjects manually entered fingerstick measurement

values for calibration into both G4 Platinum Receivers and were instructed to enter the same calibration values to both Receivers at the same time (one immediately after the other). The blinded CGM system was only used to evaluate device precision, the unblinded CGM system was considered the primary CGM system for device performance in comparison to the laboratory reference YSI.

Precision of the System was assessed and measured by the average absolute percent difference estimates and percent coefficient of variations comparing data from the two simultaneously worn sensors.

Home Portion of the Study –
The remainder of the study, time between the in-clinic sessions, took place at home. During home use, subjects performed two SMBG fingerstick measurements per day required for calibration of the system and additional fingerstick measurements as required for their diabetes management. Subjects were required to use the blood glucose meter provided to them (LifeScan OneTouch Ultra2) for all SMBG measurements obtained during the 7-day wear period. All subjects were instructed to manage their glucose levels per their routine diabetes management guidelines during home use.

Summary of Statistical Methods - Summary statistics for continuous variables include the mean, standard deviation, median, and range. All enrolled subjects who underwent device insertion were included in all analyses. The hypothesis test was conducted using a 1-sided binomial test, and a 95% confidence interval of the true percentage of paired points meeting the pre-specified accuracy criteria. These criteria, used by the sponsor, were met if the G4 measurement paired with a YSI measurement below 80 mg/dL is within 20 mg/dL of that YSI measurement. A G4 measurement paired with a YSI measurement above 80 mg/dL is considered accurate if it is within 20% of that YSI measurement. Normal approximated and bootstrapped confidence intervals were presented for the agreement proportion.

In subjects wearing two sensors concurrently, only the unblinded G4 Sensor was included in the primary efficacy endpoint analysis.

From the seventy-two (72) subjects enrolled in the study, a total of 9555 Sensor-YSI matched pairs were collected for the primary analysis. Among these data there were a total of 9093 matched pairs with both YSI and G4 CGM measurements within the System measurement range of 40 to 400 mg/dl. The study collected sufficient number of samples to satisfy the above described sample size requirements and hypothesis tests. With the observed proportion of interest of the study sample, the actual sample size provided more than 90% power for the hypothesis test.

Key Secondary endpoints -
- Mean and Median Absolute Relative Differences from YSI
- Hypoglycemia and Hyperglycemia Detection Rates
- Hypoglycemia and Hyperglycemia missed detection rates

- True Alert Rate
- False Alert Rate
- Accuracy of glucose rate of change of Sensor compared to glucose rate of change of YSI

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the study was limited to patients who met the following *inclusion criteria*:

   a. Age 18 years or older
   b. Diagnosed with diabetes mellitus
   c. Used one of the following methods for their diabetes management: a) intensive insulin therapy (IIT) with defined insulin:carbohydrate ratios and glucose correction factors; or b) non-intensive insulin therapy (non-IIT)
   d. For insulin-using subjects only – would not inject insulin or wear an insulin pump insertion set within 3 inches from the Sensor site during sensor wear
   e. Would insert Sensor(s) on their own and if asked, willing to wear 2 systems simultaneously
   f. Would use only the blood glucose meter provided for all blood glucose measurements performed during Sensor wear and not allow others to use this meter during the study
   g. Would participate in three 12-13 hour in-clinic sessions during which subjects must be willing to take 2 fingerstick measurements per hour (and additionally as indicated for diabetes management or clinical safety purposes)
   h. Would have an intravenous catheter inserted for 4 blood draws per hour over a total of 12-13 hours for each of the 3 in-clinic sessions
   i. For intensive-insulin using (IIT) subjects only – During each in-clinic session, would have their blood glucose levels manipulated into high and low glucose levels via carbohydrate consumption, meal timing, activity levels, and/or insulin dosing. (Subjects not on IIT will only be observed during each in-clinic session. These subjects would not participate in the deliberate insulin and glucose challenges and will manage their diabetes as they usually do)
   j. For subjects that exercise routinely (at least 3 times per week), would exercise for 20 to 30 minutes during each in-clinic session, if asked
   k. Would take a minimum of 7 fingerstick measurements per day during home use days (required fingerstick measurements for calibration purposes, additional for confirmatory/comparative purposes) with the meter provided
   l. Would refrain from the use of acetaminophen during Sensor wear period and the day prior to Sensor insertion
   m. Able to speak, read, and write English
   n. In the investigator's opinion, able to be compliant with provisions laid out in this protocol.

   Patients were <u>not</u> permitted to enroll in the study if they met any of the following *exclusion criteria*:

a. Have extensive skin changes/diseases that preclude wearing the required number of devices on normal skin (e.g., extensive psoriasis, recent burns or severe sunburn, extensive eczema, extensive scarring, extensive tattoos, dermatitis herpetiformis) at the proposed wear sites
b. Have a known allergy to medical-grade adhesives
c. Are pregnant, as demonstrated by a positive pregnancy test within 72 hours of Sensor insertion
d. Were on active dialysis
e. Had a hematocrit level that is less than 36% or greater than 55% at screening visit
f. Were participating in another investigational study protocol (e.g, if a subject has recently completed participation in another drug study, the subject must have completed that study at least 30 days prior to being enrolled in this study)
g. Had a history of cardiovascular disease (including, but not limited to, ischemic heart disease, peripheral vascular disease, cardiomyopathy, cerebrovascular disease, congenital heart disease, or significant arrhythmias), epilepsy, severe migraines in the past 6 months, adrenal disease, syncope, significant hypoglycemia unawareness, or a history of severe hypoglycemia (requiring emergency medical intervention) within the last 6 months
h. Had any chronic infectious disease or intercurrent illness that would interfere with their participation in the study or pose an excessive risk to study staff handling venous or capillary blood samples (e.g. HIV/AIDS, Hepatitis B or C)
i. Had a MRI scan, CT scan, or diathermy scheduled during the week of the study. If any of these procedures are required urgently during the study, subjects would notify the study staff, end their CGM session, and remove their Sensor.

2. Follow-up Schedule

At the end of the Sensor wear period (168 hours), subjects removed the Systems according to User's Guide instructions and/or training materials provided. Upon removal, all the Sensor insertion sites were examined and evaluated by the study staff. Sensors were visually inspected at the site. All used and unused Systems (including Sensor, Transmitter, and Receiver) were returned by study staff to Dexcom for examination (e.g. close examination for mechanical integrity of Sensor wires). Study investigators documented any Adverse Device Effects (including irritations) and evaluated safety issues related to system use during the study. No long-term follow up was included in this study protocol.

3. Clinical Endpoints

The primary effectiveness measurements for this study were the glucose measurements from the Dexcom G4 Platinum System and the blood glucose values measured by the YSI Analyzer during in-clinic sessions. The sponsor

defined criteria of G4 System performance was assessed as the percentage of paired points with absolute differences between G4 System results and YSI blood glucose results of ≤20 mg/dL (for YSI values ≤80 mg/dL), or with absolute relative differences of ≤20% (for YSI values >80 mg/dL).

The primary endpoint depended on the G4-YSI matched pairs that were obtained in the in-clinic sessions on days 1, 4, and 7. Subjects contributed anywhere from 6 to 150 pairs with 85% of them contributing at least 130 pairs.

Safety data of the System were also collected and characterized by the incidence and severity of Adverse Device Effects, Serious Adverse Device Events, and Unanticipated Adverse Device Effects experienced by study subjects.

B. Accountability of PMA Cohort

All 72 subjects enrolled into the study participated in the in-clinic and the home portions of the study. All enrolled subjects contributed at least one matched pair of sensor/YSI observations to the efficacy data. 66 subjects attended all three in-clinic sessions.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a continuous glucose monitoring system study performed in the US. See the following tables (Tables 3A and 3B) for a description of the demographics and baseline characteristics of the study population.

Table 3A. Subject Demographics

Category	Number of Subjects Enrolled (N=72)
Gender, N (%)	
Male	44 (61.1%)
Female	28 (38.9%)
Age (years)	
Mean	42.20
SD	13.95
Range	18.3-74.0
Race	
White	68 (94.4%)
Asian	1 (1.4%)
Black, African American, or of African Heritage	3 (4.2%)
Ethnicity	
Hispanic or Latino	8 (11.1%)
Not Hispanic or Latino	
Body Mass Index	

Mean	28.66
SD	5.78
Range	19.6 - 49.4

Table 3B. Subject Baseline Parameters

Type of Diabetes at Diagnosis	
Type I	60 (83.3%)
Type II	12 (16.7%)
Diabetes Duration (years)	
Mean	18.9
SD	11.9
Range	1 - 55
Body Mass Index	
Mean	28.66
SD	5.78
Range	19.6 - 49.4
Baseline A1c (%)	
Mean	7.70
SD	1.30
Range	5.5 - 10.7

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the 72 subjects that participated in the study. The safety data of the System were assessed by evaluation of the incidence of all Adverse Device Effects (ADEs), Serious Adverse Device Events (SADEs), and Unanticipated Adverse Device Effects (UADEs) experienced by study subjects. Adverse events (AEs) were listed in terms of severity and relationship to device. Sensor insertion site and adhesive area were examined for erythema, edema and infection. The local skin reactions from the insertion site or the adhesive were evaluated quantitatively using Draize18 classifications.

Adverse effects that occurred in the PMA clinical study:

A total of 38 Adverse Events (AEs) were reported during the study. Twenty-two of the AEs were deemed related to the device due to Sensor insertion and adhesive area irritations; all these AEs were deemed mild and were resolved or stable upon study completion.

These events included all skin irritations. Irritation resulting from use of the System Sensor was tabulated at each Sensor removal and categorized by needle insertion site and adhesive area. Any bruising, edema, and erythema observed at each area were evaluated according to Draize's scale. The following table (Table 4) summarizes the quantitative assessments (Draize's scales) of Sensor insertion and adhesive area reactions:

Table 4 Adverse Events.

AE	N (%)
Sensor Site Erythema	
Very Slightly	7 (5.8%)
Adhesive area Erythema	
Very Slightly	12 (9.9%)
Adhesive area Edema	
Very Slightly	3 (2.5%)

The following sixteen (16) other reported AEs were deemed not related to the devices: 7 mild headaches; 1 moderate headache; 1 case of a mild sore throat; 1 subject had a skin biopsy (mild) on the face to rule out skin cancer; 1 case of mild vomiting after drinking Boost (nutritional drink given during the study); 1 case of erythema @ needle insertion site; 1 case of mild emesis; 1 case of mild viral syndrome; 1 case of moderate atypical chest pain; 1 case of moderate pericarditis.

All AEs were resolved or stable at study termination.

Per protocol, the mechanical integrity of each Sensor was independently assessed after removal of the Sensor from the subcutaneous adipose tissue. There were no reports of broken Sensor wires.

No infections occurred at either insertion or adhesive areas.

No Serious Adverse Device Events (SADEs) or Unanticipated Adverse Device Effects (UADEs) occurred during the study.

2. Effectiveness Results

The primary effectiveness measurements for this study were based on the performance evaluation of the Dexcom G4 Platinum System compared to the blood glucose values measured by YSI during in-clinic sessions. Key effectiveness outcomes are presented in the following tables (Tables 5 to 17).

Agreement of System Results with Reference Readings (YSI):
Agreement between the System and blood glucose values is characterized using paired System and YSI values. The System and YSI results were compared by pairing the YSI blood glucose value to a System glucose reading that occurred immediately after the YSI 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 YSI values.

The total number of data pairs considered in this analysis was 9152. A total of 9555 Sensor-YSI matched pairs were collected in this study; however, this analysis included CGM readings that were within the measuring range of the System (40-400 mg/dL). Of these, eighty-two percent (82%) of the System readings fall within ±20 mg/dL (1.1 mmol/L) of the YSI blood glucose values (< 80 mg/dL or 4.4 mmol/L) and within ±20% of YSI blood glucose values (≥ 80 mg/dL or 4.4 mmol/L). The confidence interval (CI) used by the sponsor was considered to be the proportion of paired values meeting the 20/20 criteria (System readings falling within ±20 mg/dL of YSI for samples < 80 mg/dL glucose and within ±20% of YSI for sample ≥ 80 mg/dL glucose) which was estimated to be 82% with a CI of (78.4, 84.7).

For readings less than or equal to 80 mg/dL (4.4 mmol/L) glucose the absolute difference in mg/dL (mmol/L) between the two glucose results was calculated. For values greater than 80 mg/dL (4.4 mmol/L) the absolute percent difference (%) from the YSI values was calculated. The percentages of total readings within 15mg/dL (0.8 mmol/L) or 15%, 20 mg/dL (1.1 mmol/L) or 20%, 30 mg/dL (1.7 mmol/L) or 30%, 40 mg/dL (2.2 mmol/L) or 40% or greater than 40 mg/dL (2.2 mmol/L) or 40% were then calculated in Table 5-A and Table 5-B.

System Agreement to YSI within CGM Glucose Ranges: Table 5-A below is categorized within CGM glucose concentrations (first column) and outlines how often a reading on the CGM matched the YSI blood glucose reading.

Table 5-A. System Agreement to YSI within CGM Glucose Ranges

CGM Glucose Range mg/dL (mmol/L)	Number of paired System-YSI	Percent within 15/15% YSI	Percent within 20/20% YSI	Percent within 30/30% YSI	Percent within 40/40% YSI	Percent Greater than 40/40% YSI
Overall	9152	71%	82%	92%	97%	3%
40-60 (2.2-3.3)	512	67%	78%	88%	94%	6%
61-80 (3.4-4.4)	781	73%	85%	94%	98%	2%
81-180 (4.5-10.0)	3853	67%	78%	91%	97%	3%
181-300 (10.1-16.7)	2784	72%	84%	93%	96%	4%
301-350 (16.7-19.4)	775	82%	91%	97%	98%	2%
351-400 (19.4-22.2)	447	74%	84%	91%	95%	5%

Note: CGM readings are within 40-400 mg/dL (2.2-22.2 mmol/L).

System Agreement to YSI within YSI Glucose Ranges: Table 5-B below is categorized within YSI reference value ranges (first column) and outlines how often a CGM reading matched with the YSI blood glucose level bins.

During the clinical study, the reference YSI values outside of the System measurable range were collected. Among these samples, on 22 occasions, when the actual blood glucose concentrations (as determined by the YSI analyzer) were lower than 40 mg/dL (2.2 mmol/L), 73% of the paired CGM glucose readings were within 20 mg/dL (1.1 mmol/L) of the YSI values, and 86% of the paired CGM glucose readings were within 30 mg/dL (1.7 mmol/L) of the YSI values. On 37 occasions, when the actual blood glucose concentration (as determined by the YSI analyzer) were greater than 400 mg/dL (22.2 mmol/L), 86% of paired System readings were within 20% of the YSI values, and 100% of the paired CGM glucose readings were within 30% of the YSI values.

Table 5-B. System Agreement to YSI within YSI Glucose Ranges

YSI Glucose Range mg/dL (mmol/L)	Number of paired System-YSI	Percent within 15/15% YSI	Percent within 20/%20 YSI	Percent within 30/%30 YSI	Percent within 40/%40 YSI	Percent Greater than 40/%40 YSI
Overall	9152	71%	82%	92%	97%	3%
<40 (2.2)	22	59%	73%	86%	100%	0%
40-60 (2.2-3.3)	461	75%	87%	94%	98%	2%
61-80 (3.4-4.4)	890	69%	81%	94%	98%	2%
81-180 (4.5-10.0)	3892	65%	76%	88%	95%	5%
181-300 (10.1-16.7)	2644	74%	85%	94%	97%	3%
301-350 (16.7-19.4)	869	79%	92%	99%	100%	0%
351-400 (19.4-22.2)	337	84%	91%	98%	100%	0%
>400 (22.2)	37	86%	86%	100%	100%	0%

Note: CGM readings are within 40-400 mg/dL (2.2-22.2 mmol/L).

Agreement of CGM to YSI When CGM Reads 'Low' or 'High':
The System reports glucose concentrations between 40 and 400 mg/dL (2.2-22.2 mmol/L). When the System determines the glucose level is below 40 mg/dL (2.2

mmol/L), the Receiver displays "LOW" in Status Box. When the G4 System determines that the glucose level is above 400 mg/dL (22.2 mmol/L), the Receiver displays "HIGH" in the Status Box. Because the System does not display glucose values below 40 mg/dL (2.2 mmol/L) or above 400 mg/dL (22.2 mmol/L), the comparisons to the actual blood glucose concentrations (as determined by the YSI analyzer) when CGM is classified as "LOW" or "HIGH" are included separately in the following table (Table 6) . The table includes the numbers and the cumulative percentages when YSI values were less than certain glucose levels (for 'LOW'), and when YSI values were greater than certain glucose levels (for 'HIGH').

Table 6. Number and Percentage of YSI values when CGM readings are 'LOW' or 'HIGH'.

YSI mg/dL (mmol/L)							
CGM Readings	CGM-YSI pairs	<55 (3.1)	<60 (3.3)	<70 (3.9	<80 (4.4)	>80 (4.4)	Total
'LOW'	n	66	18	39	19	13	155
	Cumulative %	42%	54%	79%	92%	8%	
YSI mg/dL (mmol/L)							
CGM Readings	CGM-YSI pairs	>340 (18.9)	>320 (17.8	>280 (15.6)	>240 (13.3)	<240 (13.3)	Total
'HIGH'	n	189	31	18	8	2	248
	Cumulative %	76%	89%	96%	99%	41%	

Concurrence of System and Laboratory Reference Values:
The percentage of concurring CGM readings and YSI reference values were included in Table 7. This table is categorized by each CGM glucose range (first column) and describes for each range of CGM glucose readings, what percentage of paired YSI values were in the same glucose range (shaded) or in glucose ranges above and below the paired CGM readings.

Table 7. Concurrence of System Readings and YSI values.

CGM mg/dL (mmol/L)	Number of Paired CGM-YSI	Percent of matched pairs in each YSI glucose range for each Sensor glucose range YSI mg/dL (mmol/L)										
		<40 (<2.2)	40-60 (2.2-3.3)	61-80 (3.4-4.4)	81-120 (4.4-6.7)	121-160 (6.7-8.9)	161-200 (8.9-11.1)	201-250 (11.1-13.9)	251-300 (13.9-16.7)	301-350 (16.7-19.4)	351-400 (19.4-22.2)	>400 (>22.2)
<40 (<2.2)	155	6%	48%	37%	7%	1%	0%	0%	0%	0%	0%	0%
40-60 (2.2-3.3)	512	4%	49%	36%	11%	1%	0%	0%	0%	0%	0%	0%
61-80 (3.4-4.4)	781	0%	22%	51%	24%	1%	0%	0%	0%	0%	0%	0%
81-120 (4.4-6.7)	1706	0%	2%	17%	66%	13%	1%	0%	0%	0%	0%	0%
121-160 (6.7-8.9)	1492	0%	0%	1%	25%	60%	13%	2%	0%	0%	0%	0%
161-200 (8.9-11.1)	1240	0%	0%	0%	2%	28%	53%	16%	2%	0%	0%	0%
201-250 (11.1-13.9)	1181	0%	0%	0%	0%	3%	21%	51%	21%	3%	1%	0%
251-300 (13.9-16.7)	1018	0%	0%	0%	0%	0%	4%	19%	49%	24%	3%	0%
301-350 (16.7-19.4)	775	0%	0%	0%	0%	0%	0%	3%	28%	51%	16%	1%
351-400 (19.4-22.2)	447	0%	0%	0%	0%	0%	0%	3%	10%	43%	38%	7%
>400 (>22.2)	248	0%	0%	0%	0%	0%	0%	1%	6%	21%	57%	15%

Evaluation of Accuracy:

Accuracy between matched pairs was also estimated by calculating the percent difference between the System reading and the YSI value. The System and YSI values were compared by pairing the System reading that fell immediately after the YSI value was collected.

The mean percent 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 YSI 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 YSI values, but does not demonstrate whether the System is reading, on average, higher or lower than the YSI laboratory standard. The mean absolute percent difference is the average "distance" (regardless if positive or negative) between System readings and YSI values.

These accuracy measures in differences were based on 9152 paired glucose results and are summarized in the following tables (Table 8-A and Table 8-B).

Table 8-A below is categorized by CGM glucose range (first column) and demonstrated that the System read, on average, 2.9% different (Mean Percent Difference) than the reference and 13.3% absolute different (Mean Absolute Difference) than the reference values.

Table 8-A. System Difference to YSI within CGM Glucose Ranges.

CGM Glucose Ranges mg/dL (mmol/L)	# of Paired System -YSI	Mean Percent Difference (%)	Median Percent Difference (%)	Mean Absolute Percent Difference (%)	Median Absolute Percent Difference (%)
Overall	9152	2.9	1.7	13.3	9.8
40-60 (2.2-3.3)	512	-10.0 (-0.6)	-8.2 (-0.5)	13.5 (0.8)	9.7 (0.5)
61-80 (3.4-4.4)	781	-2.4 (-0.1)	-0.4 (0.0)	11.4 (0.6)	8.6 (0.5)
81-180 (4.5-10.0)	3853	4.8	3.0	13.8	9.8
181-300 (10.1-16.7)	2784	2.1	0.0	11.9	9.2
301-350 (16.7-19.4)	775	3.8	2.8	9.8	7.9
351-400 (19.4-22.2)	447	10.4	7.7	12.8	9.1

* For CGM≤ 80 mg/dL (4.4 mmol/L), the differences in mg/dL (mmol/L) are included instead of percent differences (%). Note: CGM readings are within 40 to 400 mg/dL (2.2-22.2 mmol/L), inclusive.

Table 8-B below is categorized within YSI glucose value ranges (first column) and demonstrated that the Median Percent Difference shows that half of the time the System read 1.7% or less than the YSI blood glucose values and the Median Absolute Percent Difference shows that half of the time the System read about 9.8% or less different than YSI blood glucose values.

Table 8-B. System Difference to YSI within YSI Glucose Ranges.

YSI Glucose Ranges mg/dL (mmol/L)	# of Paired System-YSI	Mean Percent Difference (%)	Median Percent Difference (%)	Mean Absolute Percent Difference (%)	Median Absolute Percent Difference (%)
Overall	9152	2.6	1.7	13.3	9.8
*<40 (2.2)	22	14.4 (0.8)	12.9 (0.7)	14.4 (0.8)	12.9 (0.7)
40-60 (2.2-3.3)*	461	7.3 (0.4)	6.3 (0.4)	11.1 (0.6)	8.8 (0.5)
61-80 (3.4-4.4)*	890	3.6 (0.2)	2.4 (0.1)	12.2 (0.7)	10.2 (0.6)
81-180 (4.5-10.0)	3892	3.8	3.0	14.0	10.1
181-300 (10.1-16.7)	2644	1.3	0.3	11.2	8.5
301-350 (16.7-19.4)	869	-1.7	-1.5	9.8	8.6
351-400 (19.4-22.2)	337	-5.8	-5.2	8.8	6.8
>400 (22.2)	37	-11	-10	11.2	10.3

For CGM≤ 80 mg/dL (4.4 mmol/L), the differences in mg/dL (mmol/L) are included instead of percent differences (%). Note: CGM readings are within 40 to 400 mg/dL (2.2-22.2 mmol/L).

Low and High Glucose Alerts: The System has programmable High and Low Glucose Alerts that can be changed by the user and a non-changeable Low Glucose Alarm set at 55 mg/dL. The labeling instructs the user to consult with their doctor to determine what alert 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 YSI results at low and high blood glucose levels and it was determined if the alert may have sounded. The System and YSI readings were compared by pairing the System reading that occurred immediately after the YSI reading was collected. There were 9555 paired System and YSI results evaluated.

Low Glucose Alert: Estimates of how well the adjustable Low Glucose Alert performed are presented below in Table 9 followed by the definitions of the terms used in the tables.

Table 9. Hypoglycemic Alert Evaluation.

Alert Level mg/dL (mmol/L)	True Alert Rate	False Alert Rate	Hypoglycemia Detection Rate	Hypoglycemia Missed Detection Rate
55 (3.1)	50%	50%	71%	29%
60 (3.3)	64%	36%	75%	25%
70 (3.9)	79%	21%	83%	17%
80 (4.4)	87%	13%	86%	14%
90 (5.0)	90%	10%	89%	11%

Hypoglycemia Alert Rate:
The Alert Rate shows how often the alert was right or wrong. The True Alert Rate is the % of time 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 time 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 Hypoglycemia Detection Rate is the % of time the blood glucose level was at or below the alert setting and device alarmed within 15 minutes before or after the blood glucose was at or below the alert settings. The Hypoglycemia Missed Detection Rate is the % of time 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.

High Glucose Alert: Estimates of how well the adjustable High Glucose Alert performed are presented in the table (Table 10) followed by the definitions of the terms used in the tables:

Table 10. Hyperglycemic Alert Evaluation.

Alert Setting mg/dL (mmol/L)	True Alert Rate	False Alert Rate	Hyperglycemia Detection Rate	Hyperglycemia Missed Detection Rate
120 (6.7)	95%	5%	98%	2%
140 (7.8)	94%	6%	97%	3%
180 (10.0)	92%	8%	97%	3%
200 (11.1)	92%	8%	97%	3%

Alert Setting mg/dL (mmol/L)	True Alert Rate	False Alert Rate	Hyperglycemia Detection Rate	Hyperglycemia Missed Detection Rate
220 (12.2)	91%	9%	95%	5%
240 (13.3)	91%	9%	94%	6%
300 (16.7)	82%	18%	86%	14%

Hyperglycemia Alert Rate:
The Alert Rate shows how often the alert was right or wrong. The True Alert Rate is the % of time 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 time 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 Detection Rate is the % of time 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 Hyperglycemia Missed Detection Rate is the % of time 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.

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 (0.9 mmol/L) or 15%, 20 mg/dL (1.1 mmol/L) or 20%, 30 mg/dL (1.7 mmol/L) or 30%, 40 mg/dL (2.2 mmol/L) or 40% and greater than 40 mg/dL (2.2 mmol/L) or 40% of the YSI values in Table 11.

Table 11. Percentage of System Readings within YSI Laboratory Values with data stratified in 2-hour increments after calibration.

Time from Calibration	Number of Paired System-YSI	Percent within 15/15%	Percent within 20/20%	Percent within 30/30%	Percent within 40/40%	Percent greater Than 40/40%
0-2 hours	1929	78%	88%	96%	98%	2%
2-4 hours	1516	69%	81%	91%	96%	4%
4-6 hours	1547	69%	79%	91%	95%	5%

Time from Calibration	Number of Paired System-YSI	Percent within 15/15%	Percent within 20/20%	Percent within 30/30%	Percent within 40/40%	Percent greater Than 40/40%
6-8 hours	1520	68%	79%	92%	97%	3%
8-10 hours	1555	71%	82%	92%	96%	4%
10-12 hours	1068	65%	77%	91%	96%	4%
12-14 hours	17	65%	76%	82%	88%	12%

Note: CGM readings are within 40 to 400 mg/dL (2.2-22.2 mmol/L).

Sensor Life and Sensor Stability:

Sensor Life: Sensors can be worn for up to 7 days (168 hours). To estimate how long a sensor will work over 7 days, 108 sensors were evaluated to determine how many days/hours of readings each sensor provided. Ninety-four percent (94%) of the sensors lasted until day 7 (145-168 hours). There were 6 (4%) sensors that ended early, four (4) of which lasted more than 3 days.

Sensor Stability: To assess the stability of sensor performance over the 7 day time period, 108 sensors were evaluated across the 7-day wear period. Performance was estimated by calculating the percentage of System readings within 15 mg/dL (0.9 mmol/L) or 15%, 20 mg/dL (1.1 mmol/L) or 20%, 30 mg/dL (1.7 mmol/L) or 30% , 40 mg/dL (2.2 mmol/L) or 40% and greater than 40 mg/dL (2.2 mmol/L)or 40% of the YSI values at the beginning (Day 1), middle (Day 4) and end (Day 7) of the System lifecycle. The average and median of the absolute percent differences are included in the table below (Table 12).

Table 12. System Sensor Stability (Accuracy over Time).

Day of Wear	Number of Paired System-YSI	Mean Absolute Percent Differences (%)	Median Absolute Percent Differences (%)	Percent within 15/15% YSI	Percent within 20/20% YSI	Percent within 30/30% YSI	Percent within 40/40% YSI	Percent greater than 40/40% YSI
Day 1	3023	16.7%	13.7%	59%	71%	86%	94%	6%
Day 4	3108	11.4%	8.2%	77%	87%	95%	98%	2%
Day 7	3021	11.9%	8.9%	76%	87%	95%	98%	2%

Note: CGM readings are within 40 to 400 mg/dL (2.2-22.2 mmol/L).

Accuracy of Rate of Glucose Change:

The percentage of concurring CGM readings and YSI values at different rates of glucose change (ROC) are described in table 13 below.

Table 13. Concurrence of CGM and YSI at different rate of changes (ROC).

CGM ROC mg/dL/min	YSI ROC (mg/dL/min) Percent of matched pairs in each YSI glucose range for each Sensor glucose range							
	(<-3)	(-3,-2)	(-2,-1)	(-1,1)	(1,2)	(2,3)	(>3)	Total
(<-3)	5 17.2%	7 24.1%	12 41.1%	5 17.2%	0 0.0%	0 0.0%	0 0.0%	29
(-3,-2)	5 7.7%	15 23.1%	24 36.9%	21 32.3%	0 0.0%	0 0.0%	0 0.0%	65
(-2,-1)	5 1.4%	31 8.9%	124 35.4%	190 54.3%	0 0.0%	0 0.0%	0 0.0%	350
(-1,1)	17 0.2%	38 0.5%	187 2.4%	7292 91.8%	317 4.0%	70 0.9%	21 0.3%	7942
(1,2)	0 0.0%	0 0.0%	1 0.2%	254 42.5%	247 41.3%	73 12.2%	23 3.8%	598
(2,3)	0 0.0%	0 0.0%	0 0.0%	77 31.4%	93 38.0%	53 21.6%	22 9.0%	245
(>3)	0 0.0%	0 0.0%	0 0.0%	10 10.3%	38 39.2%	31 32.0%	18 18.6%	97

Precision of the System Reading:

A subgroup of 36 subjects wore two Systems (one blinded) during the study to assess the Sensor precision of two Systems worn on the same patient at the same time. Imprecision was evaluated using Paired Absolute Relative Difference (PARD) and Percent Coefficient of Variation (PCV). According to the sponsor PARD is the absolute value of the blinded Sensor minus the un-blinded Sensor divided by the average of the two Sensor values. Percent coefficient of variation is the standard deviation of the two G4 Sensors divided by the average of the two Sensor values. The mean PARD of the System during the study was 9.3% with a coefficient of variation of 6.6% which demonstrates acceptable agreement.

Number of Readings Provided:

The System is capable of providing a reading up to every 5 minutes (up to 288 readings per day). For a variety of reasons, the System may not display a glucose reading and readings are "skipped." The number of actual Sensor values provided to subjects over the entire 7-day period and the corresponding percentage is summarized below in Table 14. Adjusted within each system wear-day, the System provided an average of 97% of all expected glucose readings (288) as seen in Table 15.

Table 14. Number of Readings Provided by Each Sensor over 7-Days.

% of Total Possible Readings Provided	Total Readings Provided (Min-Max)	% of Systems Providing that Number of Readings
0-25%	167-491	1.9%
26-50%	719-914	3.7%
51-75%	1267-1267	0.9%
76-100%	1811-1992	93.5%

Table 15. System Readings within Wear Days.

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	All Days (N=108)
Mean	98%	98%	98%	98%	97%	99%	95%	97%
Median	100%	100%	100%	100%	100%	100%	100%	100%
STD	5%	3%	9%	8%	10%	3%	11%	8%

Agreement and Accuracy Relative to SMBG:

During the study, agreement between the System and blood glucose values was also characterized using paired System and self-monitoring blood glucose (SMBG) meters results (see Tables 16 and 17 below). The System and SMBG values were compared by pairing the comparative SMBG value to a System glucose reading that occurred immediately after the SMBG was collected. These results characterize the performance patients expect during real-time use of the system in their daily diabetes management when comparing the system readings to their home blood glucose meter results. Both Tables (tables 16 and 17) are categorized within CGM glucose ranges (first column). CGM readings within the measuring range of the device (40-400 mg/dL glucose) are included in this analysis.

In Table 16, for the readings less than or equal to 80 mg/dL (4.4 mmol/L) glucose the absolute difference in mg/dL (mmol/L) between the two glucose results was calculated. For glucose values greater than 80 mg/dL (4.4 mmol/L) the absolute percent difference (%) from the SMBG values was calculated. The percentages of total readings within 15 mg/dL (0.8 mmol/L) or 15%, 20 mg/dL (1.1 mmol/L) or 20%, 30 mg/dL (1.7 mmol/L) or 30%, 40 mg/dL (2.2 mmol/L) or 40% or greater than 40 mg/dL (2.2 mmol/L) or 40% were then calculated.

Overall, the System read, on average, 0.3% lower (Mean Percent Difference) than SMBG values and 13.9% absolute different (Mean Absolute Difference) than the SMBG values. The Median Percent Difference showed that half of the time the System read -1.2% or less than the SMBG values and the Median Absolute Difference shows that half of the time the System read about 10.9% or less different than SMBG values (Table 16).

Table 16. System Agreement to SMBG within CGM Glucose Ranges.

CGM Glucose Ranges mg/dL (mmol/L)	Number of Paired System-SMBG	Percent within 15/15% SMBG	Percent within 20/20% SMBG	Percent within 30/30% SMBG	Percent within 40/40% SMBG	Percent greater than 40/40% SMBG
Overall	7508	69%	81%	94%	98%	2%
40-60 (2.2-3.3)	731	75%	84%	92%	96%	4%
61-80 (3.4-4.4)	968	78%	86%	95%	99%	1%
81-180 (4.5-10.0)	3141	65%	78%	93%	98%	2%
181-300 (10.1-16.7)	1960	68%	81%	94%	97%	3%
301-350 (16.7-19.4)	450	77%	88%	98%	99%	1%
351-400 (19.4-22.2)	258	75%	85%	95%	98%	2%

*For CGM ≤ 80 mg/dL (4.4 mmol/L), the differences in mg/dL (mmol/L) are included instead of percent differences (%). Note: CGM readings are within 40 to 400 mg/dL (2.2-22.2 mmol/L).

For the analysis presented in Table 17, the Mean and Median Percent Difference and the Mean and Median Absolute Percent Difference were calculated to further illustrate the comparison between CGM readings and SMBG results. Overall, the System read, on average, 0.4% lower (Mean Percent Difference) than SMBG values and 14.0% absolute different (Mean Absolute Difference) than the SMBG values. The Median Percent Difference showed that half of the time the System read -1.4% or less than the SMBG values and the Median Absolute Difference shows that half of the time the System reads about 11.0% or less different than SMBG values (Table 17).

Table 17. System Difference to SMBG within CGM Glucose Ranges.

CGM Glucose Ranges mg/dL (mmol/L)	Number of Paired System-SMBG	Mean Percent Difference (%)	Median Percent Difference (%)	Mean Absolute Percent Difference (%)	Median Absolute Percent Difference (%)
Overall	7508	-0.4	-1.4	14.0	11.0
*40-60 (2.2-3.3)	731	-9.3 (-0.5)	-8.0 (-0.4)	11.7 (0.7)	8.0 (0.4)
*61-80 (3.4-4.4)	968	-1.0 (-0.1)	1.0 (0.1)	10.7 (0.6)	8.0 (0.4)

CGM Glucose Ranges mg/dL (mmol/L)	Number of Paired System-SMBG	Mean Percent Difference (%)	Median Percent Difference (%)	Mean Absolute Percent Difference (%)	Median Absolute Percent Difference (%)
81-180 (4.5-10.0)	3141	1.4	0.0	14.2	11.0
181-300 (10.1-16.7)	1960	-0.7	-2.8	13.0	10.3
301-350 (16.7-19.4)	450	0.7	-2.6	10.5	8.6
351-400 (19.4-22.2)	258	5.0	3.0	11.9	8.6

Note: CGM readings are within 40 to 400 mg/dL (2.2-22.2 mmol/L).

3. Subgroup Analyses

G4 system performance was evaluated within study population subgroups, such as in-clinic day 1, 4 and 7 participation group, diabetes type, age (18-20 years old transitional adolescent, 21 years old and above), body mass index (BMI), Baseline HbA1C (quartile groups) and type of diabetes medication (insulin, oral agent)..

Although not powered for analysis of subpopulations, no significant differences in performance were noted based on age, BMI, ethnicity, %HbA1C, gender, or diabetes treatment.

Exercise: Forty-four (44) subjects participated in mild to moderate physical exercise activities during the in-clinic sessions. The System performance was evaluated prior to and following mild to moderate exercise. The system performance measures (MRD, MARD) were measured within each subject in reference to the laboratory standard (YSI). The mean relative difference was 1.4 % prior to exercise vs. 7.5% following exercise and the MARD was 14.1% prior to and 20.2% following exercise. However, these results are not statistically significant (Kruskal-Wallis test p-value >0.05). The blood samples were not arteiolized during this study since the participants were not wearing a heating pad during exercise. Therefore, it is not clear whether the changes that were seen during the study were due to blood sample differences or due to blood glucose levels changing rapidly due to the exercise.

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 results of the pivotal clinical study performed in this submission establish a reasonable assurance of safety and effectiveness with the Dexcom G4 Platinum System for detecting trends and tracking patterns when used as intended, as an adjuvant to blood glucose testing in subjects with diabetes mellitus. The primary effectiveness measurements for this study were based on the performance evaluation of the Dexcom G4 Platinum System compared to the blood glucose values measured by YSI during in-clinic sessions that were obtained in the in-clinic sessions spanning the wear period of the sensor (days 1, 4, and 7).

The performance data presented above (Tables 5 to 17) support the effectiveness conclusions and established the accuracy across the claimed measuring range (40 to 400 mg/dL glucose), precision, and the claimed calibration frequency (calibrate every 12 hours), the 7 day wear period for the sensor, the alarms and alerts, and the number of readings displayed in the 7 day wear period.

The clinical study data demonstrate that the G4 PLATINUM CGM System was effective in the study population designed to be reflective of the intended use population.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory data as well as on data collected in a clinical study conducted to support PMA approval as described above.

The following events are possible adverse device effects of inserting a sensor into your skin: local infection, inflammation, pain or discomfort, bleeding at the glucose sensor insertion site, bruising, itching, scarring or skin discoloration, hematoma, tape irritation, sensor or needle fracture during insertion, wear or removal. There were no infections at the sensor insertion site or adhesive areas during the clinical study and no Serious Adverse Device Events (SADEs) or Unanticipated Adverse Device Effects (UADEs) occurred during the study. The 22 device related AEs during the study were due to very slight sensor insertion and adhesive area irritations. No sensor breakage was documented in the clinical study supporting approval of this device. Reported sensor breakage rate with similar devices has been very low, however, and this study was not powered or designed to assess the rate of breakage, though all sensors were inspected for fracture after removal. The sensor has specifically been redesigned to decrease the risk of breakage.

There are risks due to missed alerts and false negative hypoglycemia and hyperglycemic readings related to patients not being alerted to the need to perform a fingerstick to detect hypoglycemia or hyperglycemia. Additionally, there is a risk associated with false alerts and false positive hypoglycemia and hyperglycemia readings related to the need to perform unnecessary fingersticks to confirm an erroneous low or high reading. However, since patients who only use blood glucose meters to manage their diabetes without the aid of a CGM would also be unaware of the need to perform additional testing to detect an abnormal blood sugar (unless they were exhibiting symptoms of an abnormal blood glucose), the risk of inaccurate results related to the use of this device is no greater than the risk of managing diabetes with a meter alone unless patients omit a blood glucose test that they would have otherwise performed if they were not using the sensor or the sensor was not reading within their target glucose range.

Inaccurate calculation of the rate of change of glucose by the CGM could prevent a patient from performing additional blood glucose tests or taking measures to stop a trend of increasing or decreasing glucose levels which could lead to serious hypoglycemia or hyperglycemia if no action is taken to stop these glucose trends. Inaccurate calculation of the rate of change of glucose could also lead to unnecessary additional blood glucose tests or inappropriate measures to stop a trend of increasing or decreasing glucose level which could result in hyperglycemia or hypoglycemia. However the risk of medical harm is limited to instances where the user relies on the rate of change calculated by the sensor without confirmation by a blood glucose meter. This risk is partially mitigated by the requirement for subjects to base treatment decisions on blood glucose levels.

C. Benefit-Risk Conclusions

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

The use of blood glucose values to manage diabetes is well-established. CGM devices of this type that complement blood glucose testing by providing an estimate of blood glucose concentrations using more continuous measurements have been available for the past decade. They are expected to aid in the 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) and provide a mechanism for alerts and alarms that may better guide blood glucose testing. For these reasons, clinical outcome data are not requested for this type of device.

This device is a next generation CGM from this company. Performance of this new System demonstrates adequate accuracy for the intended use. The reliable and timely estimation of point blood glucose concentrations, rate of change of glucose, and the tracking and trending of glucose patterns both in the short term and over several days by this device is dependent on the accuracy of the System. Adequate accuracy with

this type of device is expected to improve patients' experience with this device, may improve the device's ability to aid in the detection of hypo- and hyperglycemic episodes, and improved long-term control.

It is further expected that 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 alert/alarm functions will further aid in the early detection of hypoglycemia and hyperglycemia to aid in the prevention of serious complications form these glucose extremes.

The G4 Platinum Sensors are designed to be replaced every 7 days and used chronically. The clinical impact of long term use of these sensors was not assessed in the clinical study; however, ongoing use of CGMs may facilitate reliable and timely estimation of both point blood glucose concentration and rate of change in blood glucose and this information will aid in the prevention of extremes of glycemia.

Additional factors to be considered in determining probable risks and benefits for the Dexcom G4 Platinum Continuous Glucose Monitoring System device included the following information.

The study design for the clinical trial was typical for the evaluation of this device type and was conducted under conditions mimicking real use, including situations intended to test device performance under stressed conditions, in a representative intended use population. Results from these data are robust.

There was one protocol violation where 19 sensors were inappropriately inserted with assistance of the study staff. 89 sensors, however, were inserted without assistance of the study staff as per protocol. An analysis was performed to assess the effect of this violation and it was determined that there was no statistical significance found between the performance of the sensors that were inserted with assistance of the study staff and those inserted without assistance.

The study performed by the sponsor in support of the G4 system is typical for the evaluation of CGM devices. Children, adolescents, pregnant women, critically ill patients, and individuals on dialysis were not evaluated in this clinical trial and it is not known whether the anatomic, physiologic and metabolic characteristics unique to these populations will affect sensor performance. Therefore these results cannot be applied to these populations who are included in the limitations of use of this device. The Sponsor included subjects representative of the intended use population ages 18-70. These results, therefore could be applicable to all adults with diabetes mellitus not included in the limitations of use.

Diabetes is a chronic condition that is treatable with appropriate patient management. Persons with diabetes have the potential to live a normal life span with good control of their disease; however, many persons die prematurely or suffer disability due to complications from this disease.

Persons with diabetes treated with intensive insulin therapy need to test their blood glucose levels frequently to adjust their insulin and food intake to prevent severe hypoglycemia or hyperglycemia. Persons on less intensive insulin therapy or non-insulin therapies may not need to test their blood sugar as frequently on a day to day basis and may be less prone to severe hypoglycemia, but still have to evaluate their level of glycemia either with HbA1c levels every 3 months, fasting blood glucose levels, and/or periodic blood glucose levels other times during the day.

Persons with diabetes are at risk for microvascular disease (retinopathy, nephropathy, and neuropathy) and macrovascular disease which may cause significant morbidity and contribute to premature death. The risks of these conditions increase with duration of diabetes and magnitude of long term hyperglycemia. Patients may also develop hypoglycemia unawareness and loose the early warning symptoms of hypoglycemia. This increases the chance of severe hypoglycemia which can lead to loss of consciousness, seizures and, occasionally, death. The risk of hypoglycemia unawareness increases with duration of diabetes and frequency of less severe hypoglycemia.

Data was not presented in this submission regarding how persons tolerate the risks posed by the device. Reports in the literature indicate that not all patients continue to use these types of devices on a regular basis after initial use. Many patients cannot tolerate the false and missed alerts, the lag in interstitial glucose measurement compared to blood glucose measurement, and/or the discomfort or dislike for wearing a device constantly attached to the body. Reports also indicate that many subjects find the alerts and tracking and trending capabilities extremely helpful and are willing to tolerate the physical and analytical risks of the device to obtain the benefits.

Given the constant burden of this chronic disease to balance food, exercise, and insulin, and both the risk of short term serious complications from hypoglycaemia and long term complications from hyperglycemia, many subjects will tolerate the minimal risk of this device for its benefit.

Self blood glucose monitoring with meters is available to monitor blood glucose and continues with this device when used as indicated. The intended use of the System is to supplement blood glucose monitoring and is not a replacement for blood glucose monitoring. Blood glucose meters are very effective in evaluating blood glucose several times a day, but cannot provide continuous blood glucose readings or information about blood glucose trends during the entire day, nor can they alert users to the rate of change of blood glucose. In addition, blood glucose meters cannot alert patients of a glucose level out of range without the subject performing a test.

In conclusion, given the available information above, the data support that for detecting trends and tracking patterns in glucose levels, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The results of the pre-clinical testing and clinical trials to assess the performance of the Dexcom G4 PLATINUM Continuous Glucose Monitoring System establish reasonable assurance that this system is safe and effective for its intended use when utilized in accordance with product labeling. as an adjunct to information obtained from standard home glucose monitoring devices.

The benefits of using the System, as discussed above, outweigh the risks. In addition, the risks of using the System to determine diabetes therapy are mitigated by labeling that states that this device should not be used to adjust therapy. The labeling warns patients that they should only adjust therapy based on blood glucose measurements. The labeling further advises patients that if their CGM reading does not correspond to their symptoms of high or low blood sugar, they should not rely on the CGM reading, but should perform a blood glucose measurement. Users are further advised that if there is a discrepancy between the CGM and the blood glucose result, the user should recalibrate the CGM to improve accuracy.

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

XIII. CDRH DECISION

CDRH issued an approval order on October 5, 2012. The final conditions of approval cited in the approval order are described below.

The applicant's manufacturing facility was 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.