

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Continuous Glucose Monitoring System
Device Trade Name:	Dexcom G4 PLATINUM (Pediatric) 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/S031
Date of FDA Notice of Approval:	May 22, 2015
Priority Review:	Not applicable

The original PMA (P120005) was approved on October 5, 2012. The indications for use are as follows:

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.

Supplement 002 was approved on February 3, 2014, which expanded the indication for pediatric patients (ages 2 to 17 years) and added an alternate sensor insertion site on the upper buttocks for the pediatric population.

Supplement 018 was approved on October 21, 2014, which updated the algorithm that converts the sensor electrical signal to glucose values for the purpose of improving accuracy in the adult population.

The SSEDs to support those indications are available on the CDRH website and are incorporated by reference here. The current supplement was submitted to update the algorithm that converts sensor electrical signal to glucose values for the purpose of improving accuracy for the pediatric population (ages 2-17).

II. INDICATIONS FOR USE

The Dexcom G4 PLATINUM (Pediatric) Continuous Glucose Monitoring System is a glucose monitoring device indicated for detecting trends and tracking patterns in persons ages 2 to 17 years with diabetes. The System is intended for single patient use and requires a prescription.

The Dexcom G4 PLATINUM (Pediatric) 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 (Pediatric) 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 (Pediatric) System results should be based on the trends and patterns seen with several sequential readings over time.

III. CONTRAINDICATIONS

The following are included in the product labeling:

- Do not use the Dexcom PLATINUM (Pediatric) System in critically ill patients. It is not known how different conditions or medications common to the critically ill population may affect the performance of the system. Sensor glucose readings may be inaccurate in critically ill patients, and solely relying on the sensor glucose alerts and readings for treatment decisions could result in missing severe hypoglycemia (low blood glucose) or hyperglycemia (high blood glucose) events.
- 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 (Pediatric) 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 (Pediatric) Continuous Glucose Monitoring System User's Guide.

V. DEVICE DESCRIPTION

The current supplement is for the modification of the algorithm to the previously approved Dexcom G4 PLATINUM (Pediatric) Continuous Glucose Monitoring System. The algorithm modification is referred to as Software 505. The algorithm converts sensor electrical signal to glucose values.

The Dexcom G4 Platinum (Pediatric) Continuous Glucose Monitoring System consists of the following components: the G4 Platinum Sensor, the G4 Platinum Transmitter, and the G4 Platinum Receiver.

No modifications were made to the sensor or transmitter in this supplement. The receiver hardware has not changed. The algorithm modifications require new firmware in the receiver. Current users can download the updated receiver software onto their G4 PLATINUM (Pediatric) Receiver. The updated IFU bundle will be available by mail upon request or can be downloaded from the Dexcom website (www.dexcom.com).

Removal of warnings from Device Receiver and Labeling

As a result of the improved performance of the System in the pediatric population and hypoglycemia detection rates at glucose levels ≤ 70 mg/dL, warnings regarding accuracy and low glucose events have been removed from the user interface, Receiver Software (SW10505), Quick Start Guide (LBL012912), User's Guide (LBL012867), Tutorial (MT23000), and Training Checklist (LBL012949).

See the SSED for P120005 for a more detailed device description.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the control of diabetes. 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 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 G4 Platinum (Pediatric) System with Software 505 has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

The following are possible effects of inserting a sensor and wearing the adhesive patch: redness at the sensor insertion site, skin irritation (erythema/edema), 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.

The risk related to either an inaccurate sensor value which should be outside of the patient's target range, missed alerts, false alerts, false negative hypoglycemia and hyperglycemic readings and false positive hypoglycemia and hyperglycemia is the risk of the device not alerting the user that additional blood glucose testing with a meter should be performed, or of performing unnecessary fingersticks. Patients may rely on the CGM to alert them to low or high glucose levels rather than using blood glucose values from a meter. There is also a risk that patients that are relying on CGM values won't perform fingerstick testing as often as they would without the CGM. In both cases, blood glucose values may differ from sensor glucose readings.

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.

For the specific adverse events that occurred in the clinical studies, see Section X below and the SSED for the original PMA (P120005).

IX. SUMMARY OF PRECLINICAL STUDIES

The changes from the approved G4 Platinum (Pediatric) Continuous Glucose Monitoring System (P120005/S002) are limited to an update in the algorithm (Software 505) in the receiver. The preclinical studies included applicable software verification and validation testing. A summary of the testing performed is summarized below. Also see the original P120005 SSED for details on other preclinical studies performed that are still applicable to this modified device.

A. Laboratory Studies

Testing was performed to support the algorithm changes in the receiver firmware. The verification and validation activities were completed according to the FDA guidance entitled General Principles of Software Validation: Final Guidance for Industry and FDA Staff released January 11, 2002.

Verification 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.

Validation of the software implementation is completed and confirmed by examination and provision of objective evidence that the software end products conform to user needs and intended uses, and that the software requirements are consistently fulfilled.

B. Animal Studies

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

C. Additional Studies

None

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness with the Dexcom G4 Platinum (Pediatric) System for detecting trends and tracking patterns when used as an adjunct to blood glucose testing in pediatric subjects (ages 2 – 17) with diabetes mellitus. Data from this clinical study supported the PMA (P120005/S002) approval decision. Also see the original P120005/S002 SSED for details on this clinical study.

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the *Dexcom G4 Platinum (Pediatric) System with Software 505* (Software 505 Study) for detecting trends and tracking patterns when used as an adjunct to blood glucose testing in pediatric subjects (ages 2 – 17) with diabetes mellitus in the US under IDE #G140042. Data from this clinical study support this PMA supplement approval decision. A summary of the Software 505 study is presented below.

A. Study Design

The first subject was screened on May 20, 2014 and the final subject's participation ended on September 4, 2014. A total of 79 patients were enrolled at 5 U.S. investigational sites.

The purpose of the study was to evaluate the effectiveness and safety of the System with a modified algorithm (Software 505) when used as an adjunctive device to blood glucose testing over a 7 -day wear period in pediatric subjects (ages 2 to 17) with diabetes mellitus. This study was a non-randomized, prospective, multi-center pivotal study.

Subjects wore one system for one 7-day wear period (168 hours) on either the abdomen or the upper buttocks.

Eighty-three (83) sensors were applied, four (4) of which were replacements. Seventy-nine (79) transmitters were used, with no replacements. Seventy-nine (79) receivers were used, with no replacements.

In-Clinic Portion of Study

The primary objective was to characterize the G4 Platinum (Pediatric) System with the Software 505 algorithm performance in comparison to laboratory reference measurements (Yellow Springs Instrument 2300 STAT Plus Glucose Analyzer) on venous blood samples and against and self-monitoring blood glucose (SMBG) fingerstick measurements. There was no separate control group. The study evaluated the System performance with the abdomen and upper buttocks used as sensor

insertion sites.

The performance of the System was determined across the 7 days of sensor wear time. The study population comprised children and adolescents (ages 2 to 17) with diabetes mellitus. The study population was categorized in two age groups: Pre-school age (2 to 5 years) and school age (6 to 17 years). Seventy-nine (79) subjects were enrolled from 5 sites. Fifty-nine (59) subjects contributed at least 1 CGM-reference matched pair and are included in the primary CGM-reference efficacy analyses; Seventy-six (76) subjects contributed at least 1 CGM-SMBG matched pair and are included in the CGM-SMBG efficacy analyses. All subjects are included in the safety analyses.

In addition, subjects participated in one clinic session during the 7 -day wear period. Subjects had finger stick blood glucose measurements taken on their study meter at 30 minute intervals (± 5 minutes) for the duration of the clinic session (up to 4 hours for ages 2 -5; up to 6 hours for ages 6 - 12; and up to 12 hours for ages 13 -17). The sensors were calibrated at the beginning of the clinic session. Receivers were set to blinded mode (Display OFF) for the duration of the clinic session.

School Children (6-12 years old) and Adolescents (13-17 years old) had venous samples collected for measurement on the laboratory reference method. The clinic session for Adolescents involved having the Investigator staff manipulate blood glucose into high and low glucose levels by administration of a specific meal plan and/or insulin dosing adjustments, per protocol guidelines). Blood glucose measurements for 2-12 year old children were observational only (i.e., no manipulation was done). The groups contributing to reference samples had arterialized venous blood draws through an intravenous catheter (IV) every 15 ± 5 minutes (total volume drawn not to exceed 3 ml/kg limit) to allow for evaluation of blood glucose measurements from freshly collected plasma on the laboratory reference method .

At-Home Portion of Study

During home use, the CGM was set to unblinded mode and subjects were asked to use the study-assigned blood glucose meter (Bayer's CONTOUR® NEXT USB meter) to take fingerstick measurements for calibration of the CGM device (per labeling) and diabetes management (minimum of 7 per day). Subjects were advised to conduct daily activities as normal while wearing the System.

1. Clinical Inclusion and Exclusion Criteria

- a. Ages 2 to 17 years
- b. Diagnosed with Type 1 diabetes or Type 2 diabetes

- c. Would avoid injecting insulin or wearing an insulin pump infusion set within 3 inches of the sensor site
- d. Would wear one sensor for 168 hours (+12 hours) at home
- e. Would take a minimum of seven (7) fingersticks (FS) per day during home use (as required for System calibration and confirmatory/comparative purposes) with the study-assigned blood glucose meter
- f. Would use only the blood glucose meter and CGM System provided during sensor wear
- g. Were able to refrain from the use of acetaminophen during the sensor wear period
- h. Subject and/or guardian were able to speak, read, and write English
- i. For subjects age 13-17 only: were on Intensive Insulin Therapy (IIT) with known insulin dosing parameters
- j. Would participate in one clinic session up as follows:
 - a. For subjects ages 2-5 only:
Four (4) hours in duration, during which frequent Self- Monitored Blood Glucose (SMBG) testing would be performed.
 - b. For subjects ages 6-12 only:
Six (6) hours in duration, during which frequent venous sampling (not to exceed 3 ml/kg) and Self-Monitored Blood Glucose (SMBG) testing would be performed.
 - c. For subjects ages 13-17 only:
Twelve (12) hours in duration, during which frequent venous sampling (not to exceed 3 ml/kg) and Self- Monitored Blood Glucose (SMBG) testing would be performed with deliberate insulin and glucose challenges to induce mild to moderate hypoglycemia and hyperglycemia.

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

- a. Used acetaminophen for 24-hours prior to sensor insertion and for the 7-days of sensor wear. For subjects ages 6-17, a blood sample was drawn at the start of the clinic session to evaluate the presence of any measurable acetaminophen.
- b. Presence of extensive skin changes/diseases at sensor wear site that preclude wearing the sensor on normal skin (e.g. extensive psoriasis, recent burns or severe sunburn, extensive eczema, extensive scarring, extensive tattoos, dermatitis herpetiformis)
- c. Known allergy to medical-grade adhesives

- d. Were pregnant, demonstrated by a positive test no more than 72 hours prior to enrollment (for subjects of childbearing potential)
- e. For subjects age 13-17 only: would not use an acceptable form of contraception during the study (for sexually active subjects of childbearing potential)
- f. Participated in another investigational study protocol (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).
Note: current enrollment in another observational study, whereby the subject is in the follow-up phase and no tests/procedures are required, was not exclusionary
- g. Were on Dialysis
- h. Had scheduled Magnetic Resonance Imaging (MRI) scan, Computed Tomography (CT) scan, or diathermy during the sensor wear period
- i. Any condition that, in the opinion of the Investigator, would interfere with their participation in the study or pose an excessive risk to study staff (e.g. known history of hepatitis B or C)

For subjects ages 6 -17:

- a. Hematocrit (HCT) < 35% (females) and <38% (males) via point of care (POC) or lab measurement
- b. History of cardiovascular disease (including, but not limited to, cardiomyopathy, cerebrovascular disease, congenital heart disease, or significant arrhythmias)
- c. Diagnosis of epilepsy, adrenal disease, syncope, significant hypoglycemia unawareness
- d. Severe migraines in the past 6 months
- e. History of severe hypoglycemia (requiring emergency medical intervention) within the last 6 months.

2. Follow-up Schedule

At the end of the 7-day wear period, subjects and guardians returned to the clinic to remove the Systems by themselves according to User's Guide instructions and/or training materials provided. Study staff examined and evaluated all sensor insertion sites and adhesive sites after sensor removal. Study staff assessed for any adverse events (AEs), per protocol definitions. Device-related AEs were evaluated relative to the safety profile of the System. Study staff also visually

inspected sensors at the clinic for gross mechanical failure and documented all inspection observations.

3. Clinical Endpoints

The study characterized the performance of the System (6-17 year olds) in comparison with the laboratory reference venous sample measurements and assessed the system-reference matched pairs obtain in the in-clinic sessions.

The study also characterized the CGM performance in comparison to SMBG measurements taken for all participants (2-17 years).

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

Seventy-nine (79) subjects were enrolled from 5 sites. Fifty-nine (59) subjects (6 – 17) contributed at least 1 CGM-reference matched pair and are included in the primary CGM-reference efficacy analyses; Seventy-six (76) subjects (2 – 17) contributed at least 1 CGM-SMBG matched pair and are included in the CGM-SMBG efficacy analyses. All subjects are included in the safety analyses.

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 A and B) for a description of the demographics and baseline characteristics of the study population.

Table A. Subject Demographics

Category	Number of Subjects Enrolled (N=79)
Gender, N (%)	
Male	41 (52%)
Female	38 (48%)
Age (years)	
Mean	12.2
SD	4.6
Range	3.3 – 17.9
Race	
White	76 (96%)
Other	3 (4%)
Ethnicity	
Not Hispanic or Latino	76 (96%)
Hispanic or Latino	3 (4%)

Table B. Subject Baseline Parameters

Type of Diabetes at Diagnosis	
Type I	79 (100%)
Diabetes Duration (years)	
Mean	5.6
SD	4.2
Range	0 – 17
Body Mass Index percentile	
Age (zBMI) mean	0.71
Age (zBMI) SD	0.22
Age (zBMI) Range	0.079 – 0.987
Height (zBMI) mean	0.62
Height (zBMI) SD	0.29
Height (zBMI) Range	0.03 – 0.99
Weight (zBMI) mean	0.71
Weight (zBMI) SD	0.23
Weight (zBMI) Range	0.17 – 0.99
Baseline A1c (%)	
Mean	8.5
SD	1.5
Range	5.6 – 12.8 %

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on all subjects enrolled for whom at least one sensor was inserted for the purposes of the study. The key safety outcomes and adverse effects are reported below.

All seventy-nine (79) subjects were included in the safety analysis. There were no unanticipated adverse device effects or serious adverse events reported.

Adverse effects that occurred in the PMA clinical study:

There were ten (10) adverse events (AEs). Seven (7) AEs were Erythema affecting 7 subjects; two (2) AEs were Edema affecting 2 subjects; one (1) adverse event was reported as a study procedure-related AE (IV insertion issues during clinic session). All AEs were deemed Mild and Probably Related to Study. All AEs were resolved or were stable at study termination.

No infection, bruising or bleeding occurred at the sensor needle insertion area or the adhesive area.

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; none of the sensor wires were detached from the sensor pod after the removal.

2. Effectiveness Results

The analysis of effectiveness was based on the 2262 CGM-reference matched pairs collected within the measurement range (for CGM reading only) of 40-400 mg/dL at study completion. The primary efficacy population consisted of 59 subjects for whom at least one paired CGM-reference value was collected during the clinic session. Key effectiveness outcomes are presented in Tables 1 - 13.

Agreement Relative to Reference

Agreement was characterized using paired Dexcom G4 PLATINUM (Pediatric) System CGM values and reference values. These values were compared by pairing the reference blood glucose value to the CGM System glucose reading that occurred immediately after the reference was collected. The agreement of the CGM System to blood glucose value was assessed by calculating the percentage of CGM System readings that were within 15%, 20%, 30% and greater than 40%

of the reference values. For readings less than or equal to 80 mg/dL, the absolute difference in mg/dL between the two glucose results was calculated. For values greater than 80 mg/dL, the absolute percent difference (%) from the reference values was calculated. The percentages of total readings within 15 mg/dL or 15%, 20 mg/dL or 20%, 30 mg/dL or 30% or greater than 40 mg/dL or 40% were then calculated in Table 1 (Pediatric Original and Software 505 Study). The data were further broken down by glucose concentration range. Table 1 is categorized within CGM System glucose ranges.

Original Pediatric Study (SW10050): The total number of data pairs considered in the analysis was 2922. Of these, 68% of the CGM System readings fall within ± 20 mg/dL of the reference blood glucose values ≤ 80 mg/dL and within $\pm 20\%$ of reference blood glucose values > 80 mg/dL.

Software 505 Pediatric Study (SW10505): The total number of data pairs considered in the analysis was 2262. Of these, 91% of the CGM System readings fall within ± 20 mg/dL of the reference blood glucose values ≤ 80 mg/dL and within $\pm 20\%$ of reference blood glucose values > 80 mg/dL.

Table 1. CGM System Agreement to Reference within CGM Glucose Ranges (Pediatric Original and Software 505)

CGM Glucose Range mg/dL (mmol/L)	Study	Number of paired CGM-Ref	Percent within 15/15% Ref	Percent within 20/20% Ref	Percent within 30/30% Ref	Percent Greater than 40/40% Ref
Overall	Original	2922	55%	68%	85%	7%
	Software 505	2262	81%	91%	96%	2%
40-60 (2.2-3.3)	Original	19	63%	74%	79%	21%
	Software 505	86	54%	74%	91%	3%
61-80 (3.4-4.4)	Original	76	61%	82%	92%	4%
	Software 505	142	77%	82%	90%	3%
81-180 (4.5-10.0)	Original	1155	56%	69%	84%	6%
	Software 505	805	78%	88%	97%	1%
181-300 (10.1-16.7)	Original	1380	55%	68%	85%	7%
	Software 505	957	89%	96%	99%	1%
301-350 (16.7-19.4)	Original	206	48%	62%	80%	11%
	Software 505	209	81%	91%	94%	5%
351-400 (19.4-22.2)	Original	86	48%	61%	79%	12%
	Software 505	63	64%	81%	83%	8%

Agreement When CGM System Reads “LOW” or “HIGH”

The System reports glucose readings between 40 and 400 mg/dL. When the System determines the glucose reading is below 40 mg/dL, it displays “LOW” in the Receiver Status Box. When the System determines that the glucose reading is above 400 mg/dL, it displays “HIGH” in the Receiver Status Box. Because the System does not display glucose readings below 40 mg/dL or above 400 mg/dL, the comparisons to the actual blood glucose readings (as determined by the reference analyzer) when CGM is classified as “LOW” or “HIGH” are included separately in Table 2. The tables include the numbers and the cumulative percentages when reference values were less than certain glucose readings (for “LOW”), and when reference values were greater than certain glucose readings (for “HIGH”).

Original Pediatric Study (SW10050): When the System displayed “LOW” (13 occasions), 0% (0 out of 13) of the reference values were less than 80 mg/dL.

When the System displayed “HIGH” (70 occasions), 99% (69 out of 70) of the reference values were greater than 240 mg/dL, and 97% (68 out of 70) of the reference values were greater than 280 mg/dL.

Software 505 Pediatric Study (SW10505): When the System displayed “LOW” (16 occasions), 94% (15 out of 16) of the reference values were less than 80 mg/dL, and 63% (10 out of 18) of the reference values were less than 70 mg/dL. When the System displayed “HIGH” (24 occasions), 96% (23 out of 24) of the reference values were greater than 240 mg/dL, and 92% (22 out of 24) of the reference values were greater than 280 mg/dL.

Table 2. Number and Percentage of Reference Values When CGM Readings are “LOW” or “HIGH” (Pediatric Original and Software 505)

		Reference mg/dL (mmol/L)						
CGM Readings	Study	CGM-Ref pairs	<55 (3.1)	<60 (3.3)	<70 (3.9)	<80 (4.4)	>80 (4.4)	Total
‘LOW’	Original	n	0	0	0	0	13	13
		%	0	0	0	0	100	
	Software 505	n	3	5	10	15	1	16
		%	19	31	63	94	6	
		Reference mg/dL (mmol/L)						
CGM Readings		CGM-Ref pairs	>340 (18.9)	>320 (17.8)	>280 (15.6)	>240 (13.3)	<240 (13.3)	Total
‘HIGH’	Original	n	38	51	68	69	1	70
		%	54	73	97	99	1	
	Software 505	n	14	19	22	23	1	24
		%	58	79	92	96	4	

Concurrence of System and Laboratory Reference

Tables 3-A (**Original Study**) and 3-B (**Software 505 Study**) below are categorized by ranges of CGM glucose readings. This table describes, for each range of CGM glucose readings, what percentage of paired reference values were in the same glucose range (shaded) or in glucose ranges above and below the paired CGM readings. For example, based on the **Software 505 Study**, when CGM readings are within 81 to 120 mg/dL, blood glucose levels should be within 81 to 120 mg/dL 69% of time.

Table 3-A. Concurrence of CGM Readings and Reference Values (Original Pediatric Study)

CGM mg/dL (mmol/L)	Number of Paired CGM-Ref	Percent of matched pairs in each Ref glucose range for each Sensor glucose range										
		Ref 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)	13	0%	0%	0%	54%	31%	15%	0%	0%	0%	0%	0%
40- 60 (2.2- 3.3)	19	0%	21%	58%	16%	5%	0%	0%	0%	0%	0%	0%
61- 80 (3.4- 4.4)	76	0%	21%	45%	30%	4%	0%	0%	0%	0%	0%	0%
81- 120 (4.4- 6.7)	338	0%	1%	20%	66%	12%	1%	0%	0%	0%	0%	0%
121- 160 (6.7- 8.9)	511	0%	0%	1%	36%	54%	7%	1%	0%	0%	0%	0%
161- 200 (8.9- 11.1)	596	0%	0%	0%	4%	40%	48%	6%	1%	0%	0%	0%
201- 250 (11.1- 13.9)	658	0%	0%	0%	1%	9%	44%	41%	5%	0%	0%	0%
251- 300 (13.9- 16.7)	432	0%	0%	0%	0%	2%	7%	50%	36%	3%	0%	2%
301- 350 (16.7- 19.4)	206	0%	0%	0%	0%	0%	2%	18%	59%	21%	0%	0%
351- 400 (19.4- 22.2)	86	0%	0%	0%	0%	0%	0%	3%	28%	50%	16%	2%
>400 (>22.2)	70	0%	0%	0%	0%	0%	0%	1%	14%	41%	36%	7%

Table 3-B. Concurrence of CGM Readings and Reference Values (Software 505 Study)

CGM mg/dL (mmol/L)	Number of Paired CGM- Ref	Percent of matched pairs in each Ref glucose range for each Sensor glucose range										
		Ref 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)	16	6%	25%	63%	6%	0%	0%	0%	0%	0%	0%	0%
40- 60 (2.2- 3.3)	86	0%	33%	60%	6%	1%	0%	0%	0%	0%	0%	0%
61- 80 (3.4- 4.4)	142	0%	8%	64%	26%	2%	0%	0%	0%	0%	0%	0%
81- 120 (4.4- 6.7)	314	0%	1%	15%	69%	13%	1%	1%	0%	0%	0%	0%
121- 160 (6.7- 8.9)	313	0%	0%	0%	15%	66%	18%	1%	0%	0%	0%	0%
161- 200 (8.9- 11.1)	355	0%	0%	0%	1%	18%	66%	15%	0%	0%	0%	0%
201- 250 (11.1- 13.9)	444	0%	0%	0%	0%	1%	17%	68%	14%	0%	0%	0%
251- 300 (13.9- 16.7)	336	0%	0%	0%	0%	0%	0%	26%	58%	16%	0%	0%
301- 350 (16.7- 19.4)	209	0%	0%	0%	0%	0%	0%	4%	40%	46%	9%	0%
351- 400 (19.4- 22.2)	63	0%	0%	0%	0%	0%	0%	3%	14%	62%	21%	0%
>400 (>22.2)	24	0%	0%	0%	0%	0%	0%	4%	13%	29%	38%	17%

Accuracy Relative to Reference

Accuracy between matched pairs was also estimated by calculating the percent difference between the System reading and the reference value. For example, if the reference value is 100 mg/dL and the System reading is 90 mg/dL, a 10% difference between the System and the reference is reported. The System and reference values were compared by pairing the System reading that fell immediately after the reference value was collected.

In the example above, the System reading is less than the reference value, so the percent difference reading is negative. The mean percent difference is the average of all positive and negative percent differences between the two devices; it tells if the System reads higher or lower on average than the reference within each glucose range.

Another estimate used to show the accuracy of the System is the absolute percent difference. The absolute percent difference tells the percent difference or “distance” between the System and reference values, but does not tell whether the System is reading, on average, higher or lower than the reference laboratory standard. The mean absolute percent difference is the average “distance” (regardless if positive or negative) between System readings and reference values.

Accuracy measures in differences for both the **Original Pediatric and Software 505 Pediatric Studies** are based on 2922 and 2262 paired glucose results, respectively; the data are summarized in Table 4 below. Table 4 is categorized within CGM glucose ranges.

Original Pediatric Study (SW10050): Overall, on average, the System reads 13.5% different (Mean Percent Difference) than the reference and 17.4% absolute different (Mean Absolute Difference) than the reference values. The Median Percent Difference shows that half of the time the System reads 11.6% or less than the reference blood glucose values and the Median Absolute Percent Difference shows that half of the time the System reads about 13.5% or less than the reference blood glucose values.

Software 505 Pediatric Study (SW10505): Overall, on average, the System reads 1.8% different (Mean Percent Difference) than the reference and 10.4% absolute different (Mean Absolute Difference) than the reference values. The Median Percent Difference shows that half of the time the System reads 1.2% or less than the reference blood glucose values and the Median Absolute Percent Difference shows that half of the time the System reads about 7.9% or less than the reference blood glucose values.

Table 4. Differences between CGM System and Reference within CGM Glucose Ranges (Original Pediatric and Software 505 Study)

CGM Glucose Ranges mg/dL (mmol/L)	Study	# of Paired values for System and Reference	Mean Percent Difference (%)	Median Percent Difference (%)	Mean Absolute Percent Difference (%)	Median Absolute Percent Difference (%)
Overall	Original	2922	13.5	11.6	17.4	13.5
	Software 505	2262	1.8	1.2	10.4	7.9
40-60 (2.2-3.3)	Original	19	-18.1	-9.1	19.2	9.1
	Software 505	86	-15.3	-13.2	16.1	13.2
61-80 (3.4-4.4)	Original	76	-3.7	-2.3	13.4	10.6
	Software 505	142	-4.8	-1.0	11.8	7.7
81-180 (4.5-10.0)	Original	1155	11.9	9.7	17.0	13.0
	Software 505	805	1.9	0.7	10.6	8.1
181-300 (10.1-16.7)	Original	1380	14.8	12.4	17.4	13.3
	Software 505	957	2.2	1.0	8.1	6.5
301-350 (16.7-19.4)	Original	206	19.2	15.9	19.4	15.9
	Software 505	209	7.8	6.5	11.0	7.9
351-400 (19.4-22.2)	Original	86	18.5	15.5	19.1	15.5
	Software 505	63	14.9	11.6	15.2	11.6

Low and High Glucose Alerts

The ability of the System to detect high and low glucose levels is assessed by comparing System results to reference results at low and high blood glucose levels and determining if the alert may have sounded. The System and reference values were compared by pairing the System reading that occurred immediately after the reference value was collected. The labeling instructs the user to consult with their doctor to determine what alert settings would be best for them.

The Low Glucose Alert

Estimates of how well the adjustable Low Glucose Alert performs are presented in Tables 5-A, 5-B and 5-C below. Table 5-A represents the alert evaluation within 15 minutes of the reference value for a sub-set of the pediatric population—subjects age 6 to 17 years who had reference measurements every 15 minutes. Table 5-B represents the alert evaluation within 30 minutes of an SMBG reading for 2- to 5-year old subjects in the pediatric study.

Hypoglycemia Alert Rate

The Alert Rate shows how often the alert is right or wrong. The True Alert Rate is the percent of time the device alarmed when the blood glucose level was at or below the alert setting within 15 or 30 minutes before or after the device alarmed. The False Alert Rate is the percent of time the device alarmed when the blood glucose level was above the alert setting within 15 or 30 minutes before or after the device alarmed.

Hypoglycemia Detection Rate

The Detection Rate shows how often the device recognizes and alerts the user to an episode of hypoglycemia or how often it misses such an event. The Hypoglycemia Detection Rate is the percent of time the blood glucose level was at or below the alert setting and device alarmed within 15 or 30 minutes before or after the blood glucose was at or below the alert settings. The Hypoglycemia Missed Detection Rate is the percent of time the blood glucose was at or below the alert setting, but the device did not alarm within 15 or 30 minutes before or after the blood glucose was at or below the alert setting.

Table 5-A. Hypoglycemic Alert and Detection Rate Evaluation Compared to Reference (Original Pediatric and Software 505 Study, Ages 6-17)

Alert Level mg/dL (mmol/L)	Study	True Alert Rate	False Alert Rate	Hypoglycemia Detection Rate	Hypoglycemia Missed Detection Rate
55 (3.1)	Original	0%	100%	0%	100%
	Software 505	22%	78%	75%	25%
60 (3.3)	Original	11%	89%	25%	75%
	Software 505	42%	58%	78%	22%
70 (3.9)	Original	47%	53%	50%	50%
	Software 505	68%	32%	75%	25%
80 (4.4)	Original	55%	45%	55%	45%
	Software 505	86%	14%	91%	9%
90 (5.0)	Original	69%	31%	62%	38%
	Software 505	90%	10%	93%	7%
100 (5.6)	Original	75%	25%	62%	38%
	Software 505	91%	9%	93%	7%

Table 5-B. Hypoglycemic Alert and Detection Rate Evaluation Compared to SMBG (Original Pediatric and Software 505 Study, Ages 2-5)

Alert Level mg/dL (mmol/L)	Study	True Alert Rate	False Alert Rate	Hypoglycemia Detection Rate	Hypoglycemia Missed Detection Rate
55 (3.1)	Original	3%	97%	57%	43%
	Software 505	25%	75%	10%	0%
60 (3.3)	Original	11%	89%	62%	38%
	Software 505	20%	80%	10%	0%
70 (3.9)	Original	29%	71%	77%	23%
	Software 505	20%	80%	10%	0%
80 (4.4)	Original	35%	65%	85%	15%
	Software 505	61%	39%	10%	0%
90 (5.0)	Original	51%	49%	89%	11%
	Software 505	78%	22%	10%	0%
100 (5.6)	Original	64%	36%	91%	38%
	Software 505	82%	18%	10%	0%

The High Glucose Alert

Estimates of how well the adjustable High Glucose Alert performs are presented in Tables 6-A, 6-B and 6-C below. Table 6-A represents the alert evaluation within 15 minutes of the reference value for a sub-set of the pediatric population—subjects age 6 to 17 years who had reference measurements every 15 minutes. Table 6-B represents the alert evaluation within 30 minutes of an SMBG reading for 2- to 5-year old subjects in the pediatric study.

Hyperglycemia Alert Rate

The Alert Rate shows how often the alert is right or wrong. The True Alert Rate is the percent of time the device alarmed when the blood glucose level was at or above the alert setting within 15 or 30 minutes before or after the device alarmed. The False Alert Rate is the percent of time the device alarmed when the blood glucose level was below the alert setting within 15 or 30 minutes before or after the device alarmed.

Hyperglycemia Detection Rate

The Detection Rate shows how often the device recognizes and alerts the user to an episode of hyperglycemia or how often it misses such an event. The Hyperglycemia Detection Rate is the percent of time the blood glucose level was at or above the alert setting and the device alarmed within 15 or 30 minutes before or after the blood glucose was at or above the alert settings. The Hyperglycemia Missed Detection Rate is the percent of time the blood glucose was at or above the alert setting, but the device did not alarm within 15 or 30 minutes before or after the blood glucose was at or above the alert setting.

Table 6-A. Hyperglycemic Alert and Detection Rate Evaluation Compared to Reference (Original Pediatric and Software 505 Study, Ages 6-17)

<u>Alert Level</u> mg/dL (mmol/L)	Study	True Alert Rate	False Alert Rate	Hypoglycemia Detection Rate	Hypoglycemia Missed Detection Rate
120 (6.7)	Original	91%	9%	98%	2%
	Software 505	98%	2%	99%	1%
140 (7.8)	Original	87%	13%	99%	1%
	Software 505	97%	3%	98%	2%
180 (10.0)	Original	75%	25%	99%	1%
	Software 505	94%	6%	98%	2%
200 (11.1)	Original	71%	29%	98%	2%
	Software 505	94%	6%	97%	3%
220 (12.2)	Original	67%	33%	97%	3%
	Software 505	93%	7%	96%	4%
240 (13.3)	Original	62%	38%	96%	4%
	Software 505	88%	12%	94%	6%
300 (16.7)	Original	43%	57%	93%	7%
	Software 505	69%	31%	84%	16%

Table 6-B. Hyperglycemic Alert and Detection Rate Evaluation Compared to SMBG (Original Pediatric and Software 505 Study, Ages 2-5)

Alert Level mg/dL (mmol/L)	Study	True Alert Rate	False Alert Rate	Hypoglycemia Detection Rate	Hypoglycemia Missed Detection Rate
120 (6.7)	Original	92%	8%	98%	2%
	Software 505	97%	3%	99%	1%
140 (7.8)	Original	90%	10%	98%	2%
	Software 505	98%	2%	10%	0%
180 (10.0)	Original	87%	13%	96%	4%
	Software 505	99%	1%	93%	7%
200 (11.1)	Original	85%	15%	96%	4%
	Software 505	98%	2%	93%	7%
220 (12.2)	Original	81%	19%	95%	5%
	Software 505	10%	0%	97%	3%
240 (13.3)	Original	80%	20%	95%	5%
	Software 505	99%	1%	98%	2%
300 (16.7)	Original	71%	29%	90%	10%
	Software 505	95%	5%	96%	4%

Calibration Stability

The System must be calibrated every 12 hours. To demonstrate performance of the System over a 12-hour calibration period, Systems were evaluated to verify that performance remains consistent over the 12-hour calibration period. Systems were evaluated in 2-hour increments after calibration. Performance was estimated at each 2-hour interval and stratified by glucose values by calculating the percentage of System readings within 15 mg/dL or 15%, 20 mg/dL or 20%, 30 mg/dL or 30% and greater than 40 mg/dL or 40% of the reference values in Table 7.

Table 7. Percentage of System Readings within Reference (Ref) Values with Data Stratified in 2-hour Increments after Calibration

Time from Calibration	Study	Number of Paired System-Ref	Percent within 15/15%	Percent within 20/20%	Percent within 30/30%	Percent greater Than 40/40%
0-2 hours	Original	648	65%	75%	87%	7%
	Software 505	545	83%	91%	97%	1%
2-4 hours	Original	649	51%	67%	86%	7%
	Software 505	460	72%	89%	96%	2%
4-6 hours	Original	630	51%	61%	80%	10%
	Software 505	428	77%	88%	95%	2%
6-8 hours	Original	409	52%	68%	85%	5%
	Software 505	325	88%	92%	94%	3%
8-10 hours	Original	296	53%	69%	84%	7%
	Software 505	305	86%	93%	97%	1%
10-12 hours	Original	253	58%	74%	89%	5%
	Software 505	198	89%	94%	98%	0%
12-14 hours	Original	37	32%	38%	65%	22%
	Software 505	1	100%	100%	100%	0%

Sensor Stability Relative to Reference

Sensors can be worn for up to 7 days. To verify sensor performance over time, 176 subjects were evaluated with the **Original** Pediatric System across the 7-day wear period while 79 subjects were evaluated with the **Software 505** Pediatric System across the 7-day wear period in the pediatric studies. Performance was estimated by calculating the percentage of System readings within 15 mg/dL or 15%, 20 mg/dL or 20%, 30 mg/dL or 30% and greater than 40 mg/dL or 40% of the reference 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 Table 8 showing consistent accuracy and sensor stability over the 7-day life of the sensor.

Table 8. System Sensor Stability Relative to Reference (Ref) (Accuracy over Time, Original Pediatric and Software 505 Study)

Day of Wear	Study	Number of Paired System-Ref	Mean Absolute Percent Differences (%)	Median Absolute Percent Differences (%)	Percent within 15/15% Ref	Percent within 20/20% Ref	Percent within 30/30% Ref	Percent greater than 40/40% Ref
Day 1	Original	1016	21.2%	15.8%	48%	61%	78%	15%
	Software 505	740	12.7%	8.5%	75%	83%	91%	4%
Day 4	Original	810	16.0%	13.9%	52%	66%	87%	3%
	Software 505	795	8.1%	6.7%	89%	97%	100%	0%
Day 7	Original	1096	15.1%	11.3%	63%	76%	89%	4%
	Software 505	727	10.4%	8.4%	80%	91%	98%	1%

Precision of System Readings

In the **Original** Pediatric Study, all subjects wore two Systems. This was to look at how similarly two Systems function on the same subject (sensor precision). Precision was evaluated by comparing the glucose readings from the two Systems worn on the same subject at the same time. Results showed that System readings from the two sensors generally agreed with each other within 10% (absolute percent difference) with a 7% coefficient of variation. Only one System was worn in the **Software 505** Pediatric Study, so precision data was not collected in this study.

Sensor Life

Sensors may be worn for up to 7 days (168 hours). To estimate how long a sensor will work over 7 days, 351 sensors were evaluated in the **Original** Pediatric Study to determine how many days/hours of readings each sensor provided. Eighty-five percent (85%) of the sensors lasted until Day 7 (145-168 hours). For the **Software 505** Pediatric Study, 77 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).

Number of Readings Provided

The System is capable of providing a reading up to every 5 minutes, or up to 288 readings per day. For a variety of reasons, the System may not display a glucose

reading and readings are “skipped.” Table 9 estimates the number of readings expected to be received from the System over the entire 7-day period after calibration. For the **Original Pediatric** Study, 86% of Systems provided between 1,518 and 1,992 valid glucose readings (or more than 75% of the expected number of readings). Adjusted within each system wear-day, the **Original Pediatric** System provided an average of 95% of all expected glucose readings as seen in Table 9.

For the **Software 505 Pediatric** Study, 91% of Systems provided between 1,623 and 1,990 valid glucose readings (or more than 75% of the expected number of readings). Adjusted within each system wear-day, the **Software 505 Pediatric** System provided an average of 95% of all expected glucose readings (288) as seen in Table 10.

Table 9. Number of Readings Provided by Each Sensor over 7-Days (Original Pediatric and Software 505 Study).

% of Total Possible Readings Provided	Study	Total Readings Provided (Min-Max)	% of Systems Providing that Number of Readings
0-25%	Original	103-427	2.6%
	Software 505	60-223	4%
26-50%	Original	569-954	2.6%
	Software 505	877-891	3%
51-75%	Original	1006-1484	8.5%
	Software 505	1131-1342	3%
76-100%	Original	1518-1992	86.2%
	Software 505	1623-1990	91%

Table 10. System Readings within Wear Days (Original Pediatric and Software 505 Study).

	Study	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	All Days (N=77)
Mean	Original	97%	96%	96%	95%	94%	94%	92%	95%
	Software 505	96%	96%	95%	96%	93%	95%	93%	95%
Median	Original	99%	99%	99%	99%	99%	99%	98%	99%
	Software 505	99%	98%	99%	99%	97%	97%	98%	98%
STD	Original	6%	10%	9%	12%	14%	14%	17%	12%
	Software 505	9%	6%	12%	10%	15%	7%	12%	11%

Agreement and Accuracy Relative to SMBG

During the study, agreement between the System and SMBG results was also characterized using paired System and SMBG results (Tables 11-12 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 value was obtained. These results characterize the performance subjects 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.

Tables 11 is categorized within CGM glucose ranges. For readings less than or equal to 80 mg/dL the absolute difference in mg/dL between the two glucose results was calculated. For values greater than 80 mg/dL the absolute percent difference (%) from the SMBG values was calculated. The percentages of total readings within 15 mg/dL or 15%, 20 mg/dL or 20%, 30 mg/dL or 30%, or greater than 40 mg/dL or 40% were then calculated. For example, if the CGM reads 100 mg/dL, it is between 81-180 mg/dL range the CGM readings should be within 20% of the SMBG values 74% of the time for the **Original** Pediatric System and 84% time for the **Software 505** Pediatric System.

Table 11. System Agreement to SMBG within CGM Glucose Ranges (Pediatric Original and Software 505)

CGM Glucose Range mg/dL (mmol/L)	Study	Number of paired CGM-Ref	Percent within 15/15% Ref	Percent within 20/20% Ref	Percent within 30/30% Ref	Percent Greater than 40/40% Ref
Overall	Original	16318	64%	76%	89%	5%
	Software 505	4264	73%	84%	94%	2%
40-60 (2.2-3.3)	Original	487	44%	55%	68%	19%
	Software 505	240	54%	71%	86%	7%
61-80 (3.4-4.4)	Original	1340	59%	70%	85%	7%
	Software 505	399	64%	76%	92%	2%
81-180 (4.5-10.0)	Original	7084	62%	74%	90%	5%
	Software 505	1650	72%	84%	95%	2%
181-300 (10.1-16.7)	Original	5627	69%	80%	90%	5%
	Software 505	1526	79%	89%	97%	2%
301-350 (16.7-19.4)	Original	1176	65%	77%	90%	4%
	Software 505	319	72%	83%	94%	2%
351-400 (19.4-22.2)	Original	604	58%	72%	86%	6%
	Software 505	130	69%	79%	86%	8%

Table 12 is categorized within CGM glucose ranges. Overall, the System in the **Original** Pediatric Study read, on average, 2.2% higher (Mean Percent Difference) than SMBG values and 15.3% absolute different (Mean Absolute Percent Difference) than the SMBG values. The Median Percent Difference shows that half of the time the System reads 0.9% or less than the SMBG values and the Median Absolute Percent Difference shows that half of the time the System reads about 11.1% or less different than SMBG values.

Overall, the System in the **Software 505** Pediatric Study reads, on average, 0.7% lower (Mean Percent Difference) than SMBG values and 12.5% absolute different (Mean Absolute Percent Difference) than the SMBG values. The Median Percent Difference shows that half of the time the System reads -1.1% or less than the SMBG values and the Median Absolute Percent Difference shows that half of the time the System reads about 9.5% or less different than SMBG values.

Table 12. System Difference to Reference (Ref) within CGM Glucose Ranges (Original Pediatric and Software 505 Study)

CGM Glucose Ranges mg/dL (mmol/L)	Study	# of Paired System-Ref	Mean Percent Difference (%)	Median Percent Difference (%)	Mean Absolute Percent Difference (%)	Median Absolute Percent Difference (%)
Overall	Original	16318	2.2	0.9	15.3	11.0
	Software 505	4264	-0.7	-1.1	12.5	9.5
40-60 (2.2-3.3)	Original	487	-22.1	-17.0	23.9	18.0
	Software 505	240	-15.9	-14.0	16.9	14.0
61-80 (3.4-4.4)	Original	1340	-11.8	-8.0	17.0	11.0
	Software 505	399	-7.8	-6.0	13.7	10.0
81-180 (4.5-10.0)	Original	7084	1.1	-1.0	15.4	11.4
	Software 505	1650	-1.2	-2.6	12.1	9.5
181-300 (10.1-16.7)	Original	5627	5.7	3.4	13.5	9.5
	Software 505	1526	1.7%	0.9%	10.1%	7.7%
301-350 (16.7-19.4)	Original	1176	9.6	7.2	14.2	10.4
	Software 505	319	6.7	5.9	11.8	8.9
351-400 (19.4-22.2)	Original	604	12.7	10.2	16.1	11.9
	Software 505	130	12.0	8.9	15.7	10.6

Sensor Stability Relative to SMBG

Sensors can be worn for up to 7 days. Performance was estimated by calculating the percentage of system readings within various percentages of the SMBG values at each day of the sensor wear period (Table 13). The average and median of the absolute percent differences are included in the tables.

Table 13. System Sensor Stability Relative to SMBG (Accuracy over Time, Original Pediatric and Software 505 Study)

Day of Wear	Study	Number of Paired System-SMBG	Mean Absolute Percent Differences (%)	Median Absolute Percent Differences (%)	Percent within 15/15% SMBG	Percent within 20/20% SMBG	Percent within 30/30% SMBG	Percent greater than 40/40% SMBG
Day 1	Original	3216	18.8%	14.2%	53%	65%	81%	10%
	Software 505	893	14.8%	10.7%	64%	79%	91%	5%
Day 2	Original	2148	16.2%	12.4%	60%	74%	87%	6%
	Software 505	436	13.2%	10.4%	69%	81%	95%	3%
Day 3	Original	1977	15.2%	11.0%	63%	76%	89%	5%
	Software 505	441	13.8%	11.3%	66%	77%	91%	2%
Day 4	Original	2830	14.0%	10.9%	66%	79%	91%	4%
	Software 505	850	10.7%	8.5%	79%	91%	97%	1%
Day 5	Original	1768	15.4%	10.7%	67%	78%	90%	5%
	Software 505	374	11.4%	8.7%	74%	86%	96%	1%
Day 6	Original	1704	14.3%	9.8%	68%	79%	90%	4%
	Software 505	410	12.3%	9.2%	72%	80%	93%	2%
Day 7	Original	2675	12.4%	9.2%	72%	83%	94%	3%
	Software 505	860	11.3%	8.6%	79%	90%	96%	2%

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 5 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

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

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

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 of the Dexcom G4 Platinum (Pediatric) System using the modified algorithm (Software 505) for detecting trends and tracking patterns when used as intended, as an adjuvant to blood glucose testing in subjects ages 2 – 17 with diabetes mellitus. The primary effectiveness measurements for this study were based on the performance evaluation of the Dexcom G4 Platinum (Pediatric) System compared to the blood glucose values measured by the reference analyzer 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 1 - 13) 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 (Pediatric) CGM System with Software 505 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 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 the user's skin: local infection, inflammation, pain or discomfort, bleeding at the glucose insertion site, bruising, itching, scarring or skin discoloration, hematoma, tape irritation, sensor or needle fracture during insertion, wear or removal. All seventy-nine (79) subjects were included in the safety analysis. There were no infections at the sensor insertion site or adhesive areas during the clinical study and no Serious

Adverse Device Events or Unanticipated Adverse Device Effects occurred during the study. The device related AEs during the study were due to sensor insertion and adhesive area irritations and to pain/discomfort during the wear period. 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 were ten (10) adverse events (AEs). Seven (7) AEs were Erythema affecting 7 subjects; two (2) AEs were Edema affecting 2 subjects; one (1) adverse event was reported as a study procedure-related AE (IV insertion issues during clinic session). All AEs were deemed Mild and Probably Related to Study. All AEs were resolved or were stable at study termination.

No infection, bruising or bleeding occurred at the sensor needle insertion area or the adhesive area.

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, nor any sensor wire detachments from the sensor housing units.

No serious adverse effects or unanticipated adverse device effects were reported in the clinical studies. However, there are risks related to either an inaccurate sensor value outside of the patient's normal range or a false alert/alarm that results in performing an unnecessary additional blood glucose test to confirm the erroneous sensor reading. The risk of medical harm is, however, mitigated through labeling which emphasizes that patients should confirm all CGM readings prior to making treatment decisions.

There are risks due to missed alerts and false negative hypoglycemic and hyperglycemic readings related to patients not being alerted to the need to perform a fingerstick to detect hypoglycemia or hyperglycemia. Additionally, there is a risk associated with false alerts and false positive hypoglycemia and hyperglycemia readings related to the need to perform unnecessary fingersticks to confirm an erroneous low or high reading. 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. However as patients often do not test frequently enough with a meter to calculate the rate of change, this risk is not greater than with traditional glucose monitoring with a meter. Inaccurate estimation of the rate of change of glucose could also lead to unnecessary additional blood glucose tests or inappropriate measures to stop an incorrect trend of increasing or decreasing glucose level. 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 as well as the data collected in the original PMA (P120005).

This submission is for modification to the algorithm in the receiver of the G4 Platinum Sensor. The algorithm converts the sensor electrical signal to glucose values. The benefits and risks associated with the G4 System with Software 505 are unchanged from the Original G4 system. The sensor performance of the G4 System with Software 505 is effective for its intended use.

This device is intended to supplement self-monitoring of blood glucose to track and trend interstitial glucose levels as estimates of glucose excursions in the blood. The adjustable hypoglycemia and hyperglycemia alerts are intended to warn the patients that they need to test their blood sugar to see if they need to take action to treat or prevent a hypoglycemic or hyperglycemic event. Furthermore, CGM measurements, which are performed every 5 minutes for 7 days via an indwelling sensor, do not require repeated performance of fingersticks with a lancet for each measurement as is required for each individual blood glucose measurement with a traditional glucose meter.

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. Furthermore, real time knowledge of whether blood glucose is

increasing or decreasing adds information unavailable by traditional discrete monitoring. This information regarding direction and rate of change can alert users that they need to take action to prevent hypoglycemia or hyperglycemia. The alert functions can notify users that they need to test their blood sugar to see if they need to take action to treat asymptomatic hypoglycemia or hyperglycemia before their blood glucose concentration reaches a dangerous level. This is especially helpful for individuals with hypoglycemia unawareness (these individuals may develop severe hypoglycemia with loss of consciousness, seizures, or rarely death without the normal warning symptoms), or during the night when subjects may have prolonged hypoglycemia that does not waken them which could proceed to severe hypoglycemia if not treated in time. Traditional blood glucose monitoring is not able to capture these potentially dangerous episodes of asymptomatic hypoglycemia. Therefore, this device provides significant benefit to users not possible with traditional glucose monitoring.

A minor risk of this device is that users may need to perform unnecessary fingersticks to evaluate their blood glucose when the CGM gives false positive hypoglycemic and hyperglycemic readings or alerts. There is a minor risk of skin irritation, inflammation, or infection due to either the sensor needle or the adhesive.

There is a risk of a sensor breakage leaving a sensor fragment under the skin. This event was reported infrequently with previously approved sensors. No sensor breakage was documented in this study. 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 hypoglycemic and hyperglycemic readings related to patients not being alerted to the need to perform a fingerstick to detect hypoglycemia or hyperglycemia. There is a risk due to 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. 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.

There is a risk related to off label use of the device if patients make decisions on diabetes management based on inaccurate sensor readings alone without confirmation by blood glucose testing.

Despite the reduced accuracy in this patient population, particularly in the low glucose range, the CGM provides valuable tracking and trending information to children and their parents. If the expected performance of the device is understood, the beneficial information gained from this device outweighs the risk of missed low glucose alerts. Therefore, the strong warnings added to the labeling and receiver display explaining the differences in performance in pediatrics compared to adults and warning against relying solely on CGM alerts to detect low glucose help to mitigate the risks of poor performance.

The labeling 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.

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 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 System, as discussed above, outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on May 22, 2015. The final conditions of approval are cited in the approval order

The applicant's manufacturing facility has 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.