SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Sensor, Glucose, Invasive, Non-adjunctive

Device Trade Name: Dexcom G5 Mobile Continuous Glucose Monitoring System

Device Procode: PQF

Applicant's Name and Address: Andrew K Balo, Executive Vice President, Regulatory, Clinical, and Global Access
Dexcom, Inc.
6340 Sequence Drive
San Diego, CA, 92121

Date(s) of Panel Recommendation: July 21, 2016

Premarket Approval Application (PMA) Number: P120005/S041

Date of FDA Notice of Approval: December 20, 2016

The original PMA (P120005) was approved on October 5, 2012 for use in persons age 18 and older; and a supplement (P120005/S002) was approved on February 3, 2014 to expand the age range to persons age 2 and older. PMA Supplements (P120005/S018 and P120005/S031) for modifications to the device to alter performance were approved on October 21, 2014 and May 22, 2015 respectively. A PMA Supplement (P120005/S033) describing modifications to the device to allow data to be transmitted directly to a mobile platform was approved on August 19, 2015. Based on those submissions, the device was indicated as follows:

The Dexcom G5 Mobile Continuous Glucose Monitoring System is a glucose monitoring system indicated for detecting trends and tracking patterns in persons (age 2 and older) with diabetes. The system is intended for single patient use and requires a prescription.

The Dexcom G5 Mobile System is indicated for use as an adjunctive device to complement, not replace, information obtained from standard home glucose monitoring devices.

The Dexcom G5 Mobile 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 G5 Mobile System results should be based on the trends and patterns seen with several sequential readings over time.

The SSEDs to support previous indications are available on the CDRH website and the original PMA as well as the previous panel track supplements are incorporated by

reference here. The current supplement was submitted to expand the indications for the Dexcom G5 Mobile Continuous Glucose Monitoring System as described below.

II. INDICATIONS FOR USE

The Dexcom G5 Mobile Continuous Glucose Monitoring System (Dexcom G5) is a glucose monitoring system indicated for the management of diabetes in persons age 2 years and older. The Dexcom G5 is designed to replace fingerstick blood glucose testing for diabetes treatment decisions. Interpretation of the Dexcom G5 results should be based on the glucose trends and several sequential readings over time. The Dexcom G5 also aids in the detection of episodes of hyperglycemia and hypoglycemia, facilitating both acute and long-term therapy adjustments. The Dexcom G5 is intended for single patient use and requires a prescription.

III. CONTRAINDICATIONS

The following are included in the product labeling:

MRI/CT/ Diathermy
Remove the Dexcom G5 sensor, transmitter, and receiver before Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, or high-frequency electrical heat (diathermy) treatment.

The Dexcom G5 has not been tested during MRI or CT scans or with diathermy treatment. The magnetic fields and heat could damage the components of the Dexcom G5, which may cause it to display inaccurate blood glucose readings or may prevent alerts.

Medications
Taking medications with acetaminophen while wearing the Dexcom G5 may inaccurately raise the glucose readings generated by the Dexcom G5. The level of inaccuracy depends on the amount of acetaminophen active in your body and is different for each person. Do not rely on continuous glucose monitoring (CGM) data produced by the Dexcom G5 if you have recently taken acetaminophen.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Dexcom G5 Mobile Continuous Glucose Monitoring System labeling.

V. DEVICE DESCRIPTION

All physical components and functionality of the device (i.e., sensor, algorithm, receiver, app) described in this submission were previously approved in P120005/S033. The changes described in the submission are to the indications for use, and the labeling of the device to support the new indications.

The Dexcom G5 Mobile Continuous Glucose Monitoring System (Dexcom G5), as approved in P120005/S033, consists of a sensor, transmitter, receiver, and mobile application. The sensor is a small, flexible, coated metal filament which is inserted into subcutaneous tissue where it generates an electrical current proportional to the local glucose concentration. The sensor is held in place by an adhesive patch. The transmitter is connected to the sensor and is worn on the body. It samples the electrical current produced by the sensor and converts these measurements into glucose readings using an onboard algorithm. The transmitter uses Bluetooth Low Energy (BLE) for two-way communication with both the Dexcom G5 receiver and a BLE-enabled Apple iOS device in order to send glucose data and receive blood glucose calibration and other user inputs from these two display devices. The receiver displays the current glucose reading (which is updated every 5 minutes) and glucose trends (for up to the previous 24 hours) from the transmitter. The receiver alerts the user when glucose levels are outside of a target zone, when it is time to enter a blood glucose value to calibrate the system, and for other important system conditions. Blood glucose values for calibration are required at least twice per day and are obtained by measuring fingertip capillary blood using a conventional blood glucose monitoring device. The mobile application provides an alternative user interface to the receiver for users with a compatible Apple iOS device. It provides similar glucose display, alert, and calibration functionality to the receiver and additionally provides connectivity to the Dexcom Share service which allows Dexcom G5 users to share glucose information in real-time with up to five selected individuals.

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. Continuous glucose monitors can be used for detecting glycemic control trends and patterns as adjunctive devices to complement, not replace, information obtained from glucose meters. Automated insulin delivery devices can be used to automatically adjust insulin delivery from an insulin pump based on glucose data generated from a continuous glucose monitor.

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with their healthcare provider to select the method that best meets their needs, expectations and lifestyle.

VII. MARKETING HISTORY

The Dexcom G5 Mobile Continuous Glucose Monitoring System (P120005/S033) has been marketed in the United States and in the European Union; it was initially distributed in the US in September 2015 and in the European Union in October 2015.

The Dexcom G5 Mobile Continuous Glucose Monitoring System (P120005/S033) shares components and functionality with the Dexcom G4 PLATINUM Continuous Glucose Monitoring System, which has been available in the US since October 2012 for ages 18 and older (P120005), and since February 2014 for persons aged 2 to 17 years (P120005/S002). The Dexcom G4 PLATINUM System with Share (P120005/S028) has been available since March 2015. The Dexcom G4 PLATINUM System with Share has a Bluetooth Low Energy (BLE)-enabled receiver that allows for direct communication with the Share2 mobile application

Commercialization of this system outside of the United States began in June 2012 under the brand name Dexcom G4 Continuous Glucose Monitoring System ("G4 System") for persons aged 18 and older. Dexcom later revised the name to the Dexcom G4 PLATINUM Continuous Glucose Monitoring System ("G4 PLATINUM System"). The G4 System and G4 PLATINUM System are currently available in Australia, Austria, Bahrain, Belgium, Canada, Chile, Colombia, Czech Republic, Denmark, Finland, France, Germany, Hong Kong, Hungary, India, Ireland, Israel, Italy, Kingdom of Saudi Arabia, Kuwait, Lebanon, Lithuania, Luxembourg, the Netherlands, New Zealand, Norway, Oman, Poland, Portugal, Qatar, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, the United Arab Emirates (UAE), and the United Kingdom.

Neither the Dexcom G5 Mobile Continuous Glucose Monitoring System nor any version of the G4 PLATINUM systems (with modified algorithm, with Share) have been withdrawn form marketing for any reasons related to their safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

The following are possible adverse 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, and sensor or needle fracture during insertion, wear or removal.

There are potential adverse effects associated with making treatment decisions when glucose values and rates of change provided by the device are inaccurate. The risks of making treatment decisions based on falsely high readings include inappropriate or

excessive administration of insulin. These inappropriate treatments could increase the risk of hypoglycemia or prolong existing hypoglycemia which can result in seizures, loss of consciousness, and rarely, death. The risks of making treatment decisions based on falsely low readings include inappropriate administration of carbohydrates. These inappropriate treatments could increase the risk of hyperglycemia or prolong existing hyperglycemia, increasing exposure to long-term microvascular complications of diabetes (eye, kidney, nerve and heart disease) and acute diabetic ketoacidosis (DKA) which can result in weakness, seizures, and death. The risks of making treatment decisions based on inaccurate calculation of the rate of change of glucose levels could increase the risk of serious hypoglycemia or hyperglycemia. Inaccurate calculation of the rate of change of glucose by the device could also prevent a patient from taking measures to prevent a sustained increase or decrease in glucose levels, which could lead to serious hypoglycemia or hyperglycemia.

There are potential adverse effects associated with making acute and long-term therapy adjustments when glucose values and rates of change provided by the device are inaccurate. The risks of making therapy adjustments based on inaccurate device information include inappropriate adjustment of diabetes medication regimens. This could increase the risk of hypoglycemia and corresponding risk of seizures, loss of consciousness, and rarely, death; it may also increase the risk of hyperglycemia, increasing exposure to long-term microvascular complications of diabetes (eye, kidney, nerve and heart disease) and risk of acute diabetic ketoacidosis (DKA) which can cause weakness, seizures, and death.

Potential adverse events may also result from inaccuracies that cause a failure to trigger alerts, or cause false alerts. This may cause users to take an inappropriate action, or incorrectly take no action, and result in increased risk or prolongation of hyperglycemia or hypoglycemia.

For the specific adverse events that occurred in the clinical studies please see Section XII below and the SSEDs for P120005, P120005/S018 and P120005/S031.

IX. SUMMARY OF NONCLINICAL STUDIES

The measurement performance of the device was established in studies summarized in the SSEDs for P120005/S018 and P120005/S031. The Dexcom G5 Mobile Continuous Glucose Monitoring System is modified from the devices used in studies to support those PMA applications and the modifications were reviewed by FDA and approved in P120005/S033. These modifications and the additional minor software changes described in this current submission would not affect performance of the device for the new indication. Therefore new laboratory and animal studies were not needed.

A. Laboratory Studies

No laboratory studies were performed to support this change in indications.

B. Animal Studies

No animal studies were performed to support this change in indications.

C. Additional Studies

The applicant conducted two independent computer simulations ("meal-dosing" and "two-week" simulations) to model risks of using the Dexcom G5 Mobile Continuous Glucose Monitoring System to replace glucose monitoring for diabetes treatment decision making.

Meal-dosing simulations
These simulations considered the impact of certain variables (including device, physiological, and behavioral variables) on hypoglycemia risk and hyperglycemia risk and were primarily designed to assess the safety of pre-meal insulin dosing using the Dexcom G5 Mobile Continuous Glucose Monitoring System versus traditional blood glucose monitoring. Results of these simulations supported the availability and use of glucose threshold alerts and alarms in mitigating risks of hypo and hyperglycemia related to basing diabetes treatment decisions directly on information provided by the device.

Two-week simulations
These simulations used a computer model to compare acute safety outcomes in virtual subjects using information from either the Dexcom G5 Mobile Continuous Glucose Monitoring System or traditional blood glucose monitoring as the basis for diabetes treatment decisions. These simulations used individual virtual subjects created based on experimentally-derived physiological data. Virtual subjects were assigned physiological parameters spanning the observed inter-individual variability of key diabetes-related metabolic parameters and simulated behaviors related to diabetes management and assessed for incidence and rate of hypoglycemia, hyperglycemia, and euglycemia over a two week period. Results of the simulations were not inconsistent with the safe and effective use of the device for making diabetes treatment decisions.

Information regarding these computer simulations was presented to members of the Clinical Chemistry and Toxicology Advisory Panel convened on July 21, 2016 in written Executive Summaries and oral presentations by FDA and the applicant. Advisory Panel members generally concluded that the results of the simulations were not helpful in informing safety and effectiveness of the device and these simulations were therefore not considered in the determination of device safety and effectiveness.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

No new clinical study was conducted to support the change in the indications for the device. The applicant previously performed clinical studies to establish the clinical measurement performance characteristics of the device, including accuracy across the claimed measuring range (40 to 400 mg/dL glucose), precision, claimed calibration

frequency (every 12 hours), the wear period for the sensor (7 days), performance of the alarms and alerts, and the number of readings displayed in the 7 day wear period. Information obtained in those studies was used to support a determination of safety and effectiveness of the device for use as an adjunctive device to complement, not replace, information obtained from standard home glucose monitoring devices. These clinical studies were conducted under IDE #G130238 and IDE #G140042 and a summary of these studies is provided in SSEDs for P1200005/S018 and P120005/S031.

This same clinical study information was also used to support a reasonable assurance of safety and effectiveness of the Dexcom G5 Mobile Continuous Glucose Monitoring System for replacement of fingerstick blood glucose monitoring for diabetes treatment decisions in the US. Data from these clinical studies, reports of significant human experience with the device, and recommendations from the Clinical Chemistry and Toxicology Advisory Panel convened on July 21, 2016 (described in Section XI below) were the basis for the PMA approval decision (see Section XII below).

A. Study Design

A summary of the clinical study designs is provided in SSEDs for P120005/S018 and P120005/S031.

B. Accountability of PMA Cohort

A summary of the cohort accountability is provided in SSEDs for P120005/S018 and P120005/S031.

C. Study Population Demographics and Baseline Parameters

A summary of the study population demographics and baseline parameters is provided in SSEDs for P120005/S018 and P120005/S031.

D. Safety and Effectiveness Results

1. Safety Results
   A summary of safety results is provided in SSEDs for P120005/S018 and P120005/S031. For other information considered for this PMA supplement, see Sections XI and XII, below.

2. Effectiveness Results
   A summary of effectiveness results is provided in SSEDs for P120005/S018 and P120005/S031. For other information considered for this PMA supplement, see Sections XI and XII, below.

3. Pediatric Extrapolation

The device is indicated for use in pediatric patients aged 2 and older based on clinical data provided in pediatric subjects. Extrapolation was not used to support approval.

E. Financial Disclosure

A summary of financial disclosure information is provided in SSEDs for P120005/S018 and P120005/S031.

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

A. Panel Meeting Recommendation

At an advisory meeting held on July 21, 2016, the Clinical Chemistry and Toxicology Devices Panel of the Medical Devices Advisory Committee voted:
8 to 2 (with no abstentions) that there is reasonable assurance the device is safe, 9 to 1 (with no abstentions) that there is reasonable assurance that the device is effective, and 8 to 2 (with no abstentions) that the benefits of the device do outweigh the risks in patients who meet the criteria specified in the proposed indication.

A summary of the panel meeting is available here:
http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/ClinicalChemistryandClinicalToxicologyDevicesPanel/ucm511565.htm

The panel did not specify any conditions of approval.

B. FDA's Post-Panel Action

During the July 21, 2016 Advisory Panel meeting, there was agreement among panel members that performance characteristics of the device were consistent with safe and effective use of the device for the proposed new indications. Panelists recognized that the device was already being used non-adjunctively by a large proportion of current users and they discussed related information presented by the public during the meeting as well as their own direct clinical and technical experience with the device. Panelists indicated that the ability to safely and effectively use information from the device would depend on the training and skill of the user in terms of interpreting and using information from the device and input provided by a competent and trained healthcare provider. In addition, some panelists, especially those that expressed some hesitation about the new indications, suggested that while evaluation of the safety and effectiveness of the device for the proposed indications would be best assessed with a clinical trial; important safety data could alternatively be collected with a robust post-market study.

FDA concurs with the recommendations of the panel and is approving this device as a replacement for fingerstick blood glucose testing for diabetes treatment decisions.

Discussion during the panel meeting was helpful in FDA's consideration of how existing clinical data and reports of significant human experience with the device could inform FDA's decision on the reasonable assurance of safety and effectiveness for the new indications.

To resolve concerns expressed by panel members FDA has reviewed device labeling to ensure that it is adequate to support safe and effective use. In particular, the labeling now includes a one page (front and back) Non-Adjunctive Beginning Treatment Decisions guide that presents users with key points related to safe non-adjunctive use of the device and advises users to develop proficiency with the device over days, weeks or months, and confidence in how the device performs for them, prior to starting to use the information from the device to make diabetes treatment decisions. The labelling now also specifically emphasizes that users should become familiar with the potential for variability in device accuracy between sensors and within any given sensor session prior to using the device to make diabetes treatment decisions. The draft final labeling provided by the applicant was found to be acceptable.

Further, FDA has worked with the applicant to develop a confirmatory clinical study for the device following approval. This study will evaluate safety of the device in the hands of naïve users over an extended period of time. It is expected to provide robust safety information about the new indications and address panelist requests for clinical studies that directly address safety.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The results of clinical studies, discussion and recommendations of the Clinical Chemistry and Toxicology Devices Panel of the Medical Devices Advisory Committee on July 21, 2016, and input provided by the public, including patients and caregivers regarding their significant experience with the device, provided a reasonable assurance of the effectiveness of the device.

Two clinical studies (performed to support approval of P120005/S018 and P1200005/S031 and summarized in SSEDs for those applications) established the point and trend accuracy of the device across the claimed measuring range (40 to 400 mg/dL glucose), the precision, the claimed calibration frequency (calibrate every 12 hours), the 7 day wear period for the sensor, the performance of the alarms and alerts, and the number of readings displayed in the 7 day wear period.

In comparison to similarly designed studies, data from the Dexcom G5 Continuous Glucose Monitoring System, in general, demonstrates better concordance of individual glucose values and glucose trends to a laboratory based blood glucose measurement method than other currently marketed CGM systems. Expert members of the Advisory Panel, during a meeting on July 21, 2016, indicated that the

established clinical performance characteristics of the device were consistent with effective use of the device as a replacement for traditional blood glucose monitoring.

In addition to discussion and recommendations from the members of the Advisory Panel, input regarding the effectiveness of the device was also provided in 85 comments to the docket for the July 21, 2016 FDA Advisory Committee meeting from patients and caregivers, including a letter signed by 8,027 patients, caregivers, and members of the diabetes community. Information related to effectiveness was also addressed in 33 spoken comments from patients, caregivers, scientists, healthcare providers, and industry and patient representatives during the public comment period of the FDA Advisory Committee meeting on July 21, 2016. Many patients discussed how non-adjunctive use of the Dexcom G5 Mobile Continuous Glucose Monitoring System has given them the freedom to live more normal day-to day lives and avoid serious hypoglycemic events. Additionally, patients commented on the burden and potential errors due to self-monitoring of blood glucose with a traditional glucose meter especially while outside of a controlled setting and for those who are blind; these burdens and potential errors would be expected to be reduced by the non-adjunctive use of CGM given the ease of viewing results from the device and the real-time alarms and alerts.

B. Safety Conclusions

The safety of the device is based on data collected in two clinical studies, input provided from members of the Clinical Chemistry and Toxicology Devices Panel of the Medical Devices Advisory Committee on July 21, 2016, and reports of significant human experience with the device provided by patients and caregivers. The clinical studies are described in SSEDs for P120005/S018 and P120005/S031.

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. There were no infections at the sensor insertion site or adhesive areas during the clinical studies and no serious adverse device events or unanticipated adverse device effects occurred. The device related adverse events during the studies 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 studies. Reported sensor breakage rate with similar devices has been very low; however, these studies was not powered or designed to assess the rate of breakage, though all sensors were inspected for fracture after removal.

In a study of 79 adult subjects (P120005/S031) there were ten adverse events. Seven adverse events were erythema affecting seven subjects; two adverse events were edema affecting two subjects; one adverse event was reported as a study procedure-related adverse event (IV insertion issues during clinic session). All adverse events were deemed 'Mild and probably related to study' and are likely related to use of the

device. In a study of 51 pediatric subjects (P120005/S018), 13 adverse events were reported, affecting ten subjects. Twelve adverse events were related to skin irritation related to the device (erythema at adhesion area or needle insertion site). All of these were rated as 'Very slight'. One adverse event was categorized as 'Other, possibly related to study'. All adverse events were resolved or were stable at study termination. No serious adverse effects or unanticipated adverse device effects were reported in the clinical studies.

In public comments to the docket and comments made during the public comment period of the FDA Advisory Committee meeting on July 21, 2016, a few patients and caregivers expressed concerns that the system was inaccurate, provided examples of inaccuracy compared to blood glucose meters, and stated that they did not believe the system was safe for insulin dosing. Some described specific conditions under which they believed the system to be unreliable or when it should not be used for diabetes treatment decisions; for example, during the first 24 hours of use or during times of rapidly changing glucose like exercise or after eating a large amount of refined carbohydrate. Device labeling advises users to develop proficiency with the use of the system and confidence in how the system performs for them prior to starting to use the information from the device to make diabetes treatment decisions. Labeling also advises users to consult with their healthcare provider regarding how they can best use the device to manage their diabetes.

During the Advisory Committee meeting on July 21, 2016, multiple panelists expressed concerns about the lack of pre-approval safety data for the new indications, but indicated that a robust study of the safety of the device once it was on the market could provide the necessary information. FDA has worked with the applicant to develop a confirmatory study of the device following approval. This study is expected to provide robust safety information about the new indications and address panelist concerns related to lack of clinical safety data.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described in SSEDs for P120005/S018 and P120005/S033 as well as the data collected in the original PMA (P120005), reports of significant human experience with the device provided by members of the public, and discussion and recommendation of members of the Clinical Chemistry and Toxicology Advisory Panel at the July 21, 2016 panel meeting.

This submission is for a change to the indications for use to allow the device to be used to replace self-monitoring of blood glucose in making diabetes treatment decisions. Glucose measurements are made by the device every 5 minutes for 7 days via an indwelling sensor and do not require repeated performance of fingersticks with a lancet as is required for each individual blood glucose measurement with a traditional glucose meter. The device provides users with an updated glucose value every 5 minutes and information on the direction and rate of change of glucose levels

based on recent measurements. The adjustable hypoglycemia and hyperglycemia alerts, and rate of change alerts, are intended to warn users that they may need to take action to treat or prevent a hypoglycemic or hyperglycemic event.

Continuous glucose measurement and real-time passive alert functionality is not available using traditional blood glucose monitoring. Blood glucose meters only provide information about discrete, intermittent blood glucose levels in response to a user-initiated action, and therefore are unable to passively monitor and provide information about patterns of glycemic excursions throughout the day and night when patients are be unable to test their blood glucose. Furthermore, real time knowledge of whether blood glucose is increasing or decreasing adds information unavailable from traditional discrete monitoring and has the potential to improve therapeutic decision making relative to intermittent blood glucose monitoring. For example, information regarding glucose level direction and rate of change can alert users to take action to prevent hypoglycemia or hyperglycemia, and to modify therapeutic decision making to account not only for a glucose value but also for how glucose levels are changing. The availability of continuous glucose monitoring and accompanying alerts 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), during times when patients are unable to easily check their blood glucose using a traditional blood glucose meter, and during the night when patients may have prolonged hypoglycemia that does not waken them and 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 or alert users to hyperglycemia or hypoglycemia in the absence of user action. Therefore, this device provides significant benefits to users not possible with traditional glucose monitoring.

Non-adjunctive use of the Dexcom G5 Mobile Continuous Glucose Monitoring System can also be expected to provide the benefit of decreased pain relative to fingerstick measurements. Additionally, insulin dosing based on results of the Dexcom G5 Mobile Continuous Glucose Monitoring System is not prone to common sources of inaccuracy of fingerstick blood glucose monitoring (e.g., lack of hand washing, improper storage of in-use test strips, etc.). The decreased daily burden of use of the Dexcom G5 Continuous Glucose Monitoring System relative to fingerstick glucose measurements can additionally have psychosocial benefit (e.g. reduced burnout and perceived stigma). For example, patients may suffer reduced burnout (becoming tired of the continuous attention required in diabetes management with negative effects on glycemic control). Patients may also experience lower perceived stigma (feelings of negativity or societal disapproval of having diabetes). Further, adherence to the recommended frequency of blood glucose self-monitoring is known to be suboptimal in many people with diabetes and the availability of non-adjunctive use of the Dexcom G5 Continuous Glucose Monitoring System could increase adoption of CGM use and allow for more effective glycemic monitoring in users who are non-adherent to their recommended blood glucose self-monitoring frequency. In

addition, these users would also access other benefits of this device (e.g. real-time alerts/alarms, trend information, continuous passive sharing of real-time glucose information, etc.) which are not available in currently marketed glucose meters used for traditional blood glucose monitoring.

Patients who provided public comment during the FDA Advisory Committee meeting on July 21, 2016 (to consider the non-adjunctive use of the Dexcom G5 CGM) spoke about how the Dexcom G5 CGM has given them the freedom to live more normal day-to day lives and avoid serious hypoglycemic events. Many members of the public stated that they (or their children or their patients) already use the Dexcom G5 CGM non-adjunctively to make treatment decisions and argued that a change to the indications would provide the benefit of better education on when and how patients should use the device for treatment decisions. Additionally, patients commented on the burden and potential errors due to self-monitoring blood glucose using a traditional glucose meter, especially while not in a controlled setting and for patients who are blind.

This device has lower overall accuracy than fingerstick blood glucose measurements and there are risks associated with non-adjunctive use of the device when information provided by the device is inaccurate. Risks from falsely high readings include inappropriate or excessive administration of insulin or failure to treat or prevent hypoglycemia. Inappropriate insulin administration, or inappropriate inaction, could increase the risk of hypoglycemia or prolong hypoglycemia which can result in seizures, loss of consciousness, or rarely, death. Risks from falsely low readings include failure to treat hyperglycemia and impending or existing diabetic ketoacidosis, which could result in coma or death. Risks of falsely low readings also include inappropriate administration of carbohydrate which could increase the risks of hyperglycemia or prolong hyperglycemia resulting in increased risks of acute or long term hyperglycemia-related complications. Inaccurate measurement of the rate of change of glucose by the device could increase the risk of serious hypoglycemia or hyperglycemia if insulin dosing is influenced by the inaccurate rate of change. However, device instructions specifically advise users not to make large changes in insulin dosing based on the rate of change.

There are also risks due to missed alerts and false negative hypoglycemic and hyperglycemic readings related to patients not being alerted to the need make a treatment decision to prevent impending or current hypoglycemia or hyperglycemia. There are risks due to false alerts and false positive hypoglycemia and hyperglycemia readings related to applying unnecessary treatment. Inaccurate calculation of the rate of change of glucose by the device could prevent a patient from taking measures to stop a trend of increasing or decreasing glucose levels which could lead to serious hypoglycemia or hyperglycemia. This could also lead patients to make inappropriate adjustments to their treatment, resulting in serious hypoglycemia or hyperglycemia.

There are additional risks associated with making acute and long-term therapy adjustments when information provided by the device is inaccurate. The risks of

making therapy adjustments based on inaccurate device information include inappropriate adjustment of diabetes medication regimens. This could increase the risk of hypoglycemia and corresponding risk of seizures, loss of consciousness, and rarely, death; it may also increase the risk of hyperglycemia, increasing exposure to long-term microvascular complications of diabetes (eye, kidney, nerve and heart disease) and risk of acute diabetic ketoacidosis (DKA) which can cause weakness, seizures, and death.

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 the clinical studies supporting this application. Reported sensor breakage rate with similar devices has been very low; however, these studies were not powered or designed to assess the rate of breakage, though all sensors were inspected for fracture after removal.

In summary, the overall accuracy of this device has significantly improved over previous generations and the performance is now adequate to support safe and effective use of the device for replacement of fingerstick testing for diabetes treatment decisions. Although the accuracy of this device is lower overall than blood glucose meters, it provides benefits not available from blood glucose meters. If the expected performance of the device is understood, the benefits of additional information gained from this device outweigh the risk of inaccurate results, rates of change, and false negative and positive alarms and alerts. Notably, the device requires twice daily calibration with a blood glucose meter; requiring that users have access to a blood glucose meter and use this meter twice per day. Each calibration of the G5 Mobile provides users with an opportunity to understand the accuracy performance of an individual sensor and assess whether there reasons not to use information from that sensor to make treatment decisions. Therefore, information in the labeling discussing the importance of proper calibration and encouraging users to develop proficiency with the device and develop confidence in how the device performs for them before starting to use the information from the device to make diabetes treatment decisions helps mitigate these risks. Since there are no general consensus guidelines on the use of glucose trend information for diabetes treatment decision making, currently, safe and effective use depends on users developing sufficient familiarity with the device to understand how to use trend information to influence their treatment decisions.

There are certain situations in which results from the device should not be used to replace self-monitoring of blood glucose for making diabetes treatment decisions. In particular, the labeling warns users not to use results from the device for treatment decisions if the device does not display a glucose value and trend information or if it provides inaccurate or inconsistent readings. Further, the labeling instructs users not to ignore symptoms of high or low glucose and obtain a fingerstick glucose value if readings from the device do not match their symptoms. The labeling also identifies

acetaminophen use as a contraindication to use of the device and instructs users not to relay on data produced by the device if they have recently taken acetaminophen. Users are also advised in the labeling that if there is a discrepancy between the device and a blood glucose result they should recalibrate the device to improve accuracy. Users are also able to perform blood glucose measurements at any time to check the performance of the system.

During a Clinical Chemistry and Toxicology Advisory Panel meeting on July 21, 2016, panelists emphasized that achieving the benefits of the Dexcom G5 Mobile Continuous Glucose Monitoring System for this indication would depend on the ability of the user to appropriately interpret and use information from the device, and also on suitable input provided by a competent healthcare provider. FDA recognizes that user skill also influences the safe and effective use of traditional blood glucose monitors; however, the Dexcom G5 Mobile Continuous Glucose Monitoring System provides different information to users relative to a traditional blood glucose monitor. For example, this device provides users with up to 288 glucose values per day in addition to glucose trend information (direction and rate of change in glucose levels) while traditional blood glucose monitors do not provide glucose trend information and are typically used 10 or fewer times per day by most users. Incorporating this large number of additional glucose values and available trend information into diabetes treatment decisions represents a fundamental shift in diabetes treatment and management strategies. Further, while the use of information from blood glucose monitors in the management of diabetes is well established, there is relatively little information, and no general consensus in the clinical community, on how glucose trend information should be used for making diabetes treatment decisions. On these points, multiple panelists discussed the importance of labeling in mitigating risks associated with the new indications. Panelists indicated that the instructions for use should be written to provide healthcare professionals and device users with adequate information to ensure safe and effective use of the device with the new indications. FDA reviewed draft final labeling to ensure that labeling was adequate to support safe and effective use.

Patient Perspectives:

An additional factor considered during review in determining probable risks and benefits for the Dexcom G5 Mobile Continuous Glucose Monitoring device was the patient perspective. This included public comments to the docket of the July 21, 2016 Advisory panel meeting which comprised 85 individual public comments posted to the docket of the July 21, 2016 Advisory Panel meeting including a letter signed by 8,027 diabetes patients, caregivers and members of the diabetes community. In addition, FDA considered perspectives provided by 23 self-identified patients or caregivers during the public comment period of the July 21, 2016 Advisory Panel meeting.

In conclusion, given the available information, for management of diabetes in persons age 2 years and older, including replacement of fingerstick blood glucose testing for

diabetes treatment decisions using the Dexcom G5 Mobile Continuous Glucose Monitoring System, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The information in this application, especially the established clinical point and trend accuracy, and reports of significant human experience with the device support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

A majority of the Advisory Panel, which considered the clinical accuracy data and information presented by FDA, Dexcom, and the public, also recommended that there is a reasonable assurance of safety and effectiveness of the device when used in accordance with the indications for use. Reservations expressed during panel deliberations related to device labeling and a study of the safety of the device once it is marketed. These have been addressed by FDA during review of device labeling and by ensuring the appropriate design of a confirmatory study of the marketed device to generate additional safety data.

The benefits of using the System, as discussed above, outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on December 20, 2016. The final conditions of approval cited in the approval order are described below.

Within 30 days of the receipt of the approval letter, the applicant must submit a PMA supplement that includes a complete protocol for the study of non-adjunctive use of the Dexcom Mobile CGM System for diabetes management to provide additional confirmatory safety outcomes data collected in a prospective evaluation of non-adjunctive continuous glucose monitoring in a statistically appropriate number of adult and pediatric patients over a follow up period adequate to evaluate key diabetes-related safety endpoints.

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

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.