SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Insulin infusion pump to be used with a continuous glucose monitoring system (CGM)

Device Trade Name: t:slim X2 Insulin Pump with Dexcom G5 Mobile CGM

Device Procode: OYC, PQF

Applicant's Name and Address: Tandem Diabetes Care, Inc.
11045 Roselle Street Suite 200
San Diego, CA 92121

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P140015/S020

Date of FDA Notice of Approval: August 25, 2017

The original PMA P140015, for the t:slim G4 Insulin Pump with Dexcom G4 Platinum CGM ("t:slim G4 System") was approved on September 8, 2015. It is indicated for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons (age 12 and older) requiring insulin. It is indicated for use as an adjunctive device to complement, not replace, information obtained from standard home glucose monitoring devices. The SSED to support the indication is available on the CDRH website and is incorporated by reference here.

The current supplement was submitted to expand the indication to include pediatric patients ages 6-11 years and change the indication from adjunctive to non-adjunctive CGM use (i.e., replace fingerstick blood glucose testing for diabetes treatment decisions). The device supported by this PMA also uses Dexcom's next generation G5 CGM. These changes to the indication are in line with the indications for the class II Tandem t:slim Insulin Delivery System (k160056, k162080) and Dexcom G5 Mobile CGM System (P120005/S041).

Tandem Diabetes Care, Inc. has a right of reference from Dexcom for the original PMA for the Dexcom G4 Platinum CGM System (P120005), and PMA supplements.

II. INDICATIONS FOR USE

The t:slim X2 Insulin Pump with Dexcom G5 Mobile CGM ("t:slim X2 System") consists of the t:slim X2 Insulin Pump paired with the Dexcom G5 Mobile Sensor and Transmitter.

The t:slim X2 Insulin Pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The t:slim X2 Insulin Pump can be used solely for continuous insulin delivery and as part of the t:slim X2 System to receive and display continuous glucose measurements from the Dexcom G5 Mobile Sensor and Transmitter.

The t:slim X2 System also includes continuous glucose monitoring (CGM) indicated for the management of diabetes. The Dexcom G5 Mobile CGM is designed to replace fingerstick blood glucose testing for diabetes treatment decisions.

The t:slim X2 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 t:slim X2 System results should be based on the trends and patterns seen with several sequential readings over time.

The t:slim X2 System is indicated for use in individuals 6 years of age and greater. The t:slim X2 System is intended for single patient use and requires a prescription. The device is indicated for use with NovoLog or Humalog U-100 insulin.

III. CONTRAINDICATIONS

The following is stated for device users in the labeling within the Contraindications Sections:

The t:slim X2 System is not intended for anyone unable or unwilling to:

- Test blood glucose (BG) levels as recommended by your healthcare provider
- Demonstrate adequate carbohydrate-counting skills (preferred, not required)
- Maintain sufficient diabetes self-care skills
- See your healthcare provider(s) regularly

You must also have adequate vision and/or hearing in order to recognize your System alerts.

The t:slim X2 Pump, Dexcom G5 Mobile Transmitter, and Dexcom G5 Mobile Sensor must be removed before Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, or diathermy treatment. Exposure to MRI, CT, or diathermy treatment can damage the System.

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 t:slim X2 Insulin Pump with Dexcom G5 Mobile CGM labeling.

V. DEVICE DESCRIPTION

The t:slim X2 Insulin Pump with Dexcom G5 Mobile CGM ("t:slim X2 System") consists of the t:slim X2 Insulin Pump (k162080) paired with the Dexcom G5 Mobile Sensor and Transmitter (P120005/S041 and P120005/S049). The Dexcom G5 Mobile Sensor and Transmitter work together to wirelessly send glucose readings to the t:slim X2 Insulin Pump.

The t:slim X2 Insulin Pump has been modified from the approved t:slim G4 Insulin Pump (P140015) to include the functionality of the approved Dexcom G5 Receiver (i.e., incorporate a Bluetooth Low Energy (BLE) radio). Additionally, the t:slim X2 System includes a secondary supplier to the pump motor/gearbox assembly (approved in P140015/S016) and a different cartridge/infusion set connector (approved in P140015/S017) compared to the t:slim G4 System. Changes to the pump software have been made to accommodate the new BLE radio and changes to the Tandem Device Updater (TDU) software (k160482, k162080), which allows remote updates of users' pumps, have been made to allow for compatibility with the G5 System hardware. No modifications have been made to the approved Dexcom G5 Sensor and Transmitter.

The Dexcom G4 Platinum CGM System was FDA approved in P120005 and the performance was altered in P120005/S018 and P120005/S031. The Dexcom G4 Platinum CGM System was updated to the Dexcom G5 Mobile CGM System (P120005/S033), which was subsequently approved by FDA for updates to G5 iOS App software and G5 transmitter firmware (P120005/S049). Tandem Diabetes Care, Inc. has received a right of reference from Dexcom to leverage the data in these submissions to support the change from the Dexcom G4 Platinum CGM to the Dexcom G5 Mobile CGM in the t:slim X2 System.

The t:slim X2 System is available as part of a pump refurbishment program, which is the same as the refurbishment program approved for the t:slim G4 System (P140015/S009) except for hardware, software, and labeling unique to the t:slim X2 System. There have been no changes in the manufacturing process.

The t:slim X2 System is also available as part of a pump replacement program, which is the same as the replacement pump program approved for the t:slim G4 System (P140015/S006) except for hardware, software, and labeling unique to the t:slim X2 System. There have been no changes in the manufacturing process.

t:slim X2 Insulin Pump

The t:slim X2 Insulin Pump ("the pump") is an ambulatory, battery operated, rate-programmable infusion pump designed for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. A custom accessory disposable cartridge is motor-driven to deliver patient programmed basal rates and boluses through an FDA-cleared infusion set into subcutaneous tissue.

The front of the t:slim X2 Insulin Pump includes a color touch screen display and incorporates various safety features to prevent the touchscreen from being inadvertently activated.

The t:slim X2 Insulin Pump includes a disposable insulin cartridge for storage of insulin. The cartridge attaches to the t:slim X2 Insulin Pump and is designed to hold up to 3 mL, or 300 units, of Humalog or NovoLog U-100 insulin. It is labeled as a single-use device and is intended to be replaced at least once every three days.

The t:slim X2 System contains an audible speaker and a vibrator to provide alarms, alerts and reminders to the user and to confirm the delivery of insulin.

A USB port is located on one end of the pump to allow for the download data to a computer or for the charging of the internal lithium polymer battery when connected with a power supply or car charger. The system provides the user with an indication of the remaining battery power on the display and alerts when the battery power is low.

Dexcom G5 Mobile Sensor

The G5 Mobile Sensor ("the Sensor") is comprised of a sensor applicator, an adhesive pad, transmitter mount (i.e., sensor pod) and the sensor probe. The G5 Mobile Sensor is a sterile, disposable device inserted by the user into the subcutaneous tissue using an applicator. The sensor pod is adhered to the surface of the skin with a standard medical grade adhesive pad. The applicator contains a 26-gauge introducer needle that contains the sensor probe. The applicator inserts the wire under the user's skin. After deployment, the applicator is detached and disposed of by the user, exposing a sensor pod ready for placement of the G5 Mobile Transmitter.

The sensor probe remains beneath the surface of the skin and uses the enzyme glucose oxidase to convert the glucose in the interstitial fluid around the Sensor into an electrical current proportional to the ambient glucose concentration. The Sensor may be worn for up to 7 days before being replaced with a new sensor.

Dexcom G5 Mobile Transmitter

After Sensor insertion and removal of the applicator, the user manually places the Transmitter into the transmitter mount on the adhesive pad already attached to the skin. The Transmitter is a miniature Bluetooth Low Energy (BLE) radio transmitter operating at an internationally-accepted radiofrequency. The Transmitter contains all the electrical circuitry necessary for the operation of the electrochemical Sensor and also all the radiofrequency circuitry necessary to transmit the Sensor signal via BLE to the t:slim X2

Pump. The Transmitter collects the small electrical current from the Sensor and transmits the Sensor signal wirelessly to the t:slim X2 Insulin Pump at regular 5-minute intervals. A unique Transmitter ID must be entered into the t:slimX2 Pump to activate radiofrequency communication with the Transmitter, which allows the Sensor glucose readings to be displayed on the t:slim X2 System graphical user interface. The Transmitter is reusable and can be used for repeated 7-day sessions by a single-user over the lifetime of the battery encased in the device. The Transmitter battery lasts for at least 3 months.

Dexcom G5 Mobile Sensor and Transmitter are manufactured, labeled and distributed by Dexcom. These components are identical (including their instructions) when they are sold as part of Dexcom's CGM system and when they are used as part of the t:slim X2 System. Thus, these components will be shipped under the Dexcom label and will not be explicitly labeled as part of the t:slim X2 System. The user guide for the t:slim X2 System will be provided with the t:slim X2 Pump. That user guide explains how to combine the components.

Accessories

In addition to the above described primary components of the device, the t:slim X2 System can be used with the accessories listed below:

- Becton Dickinson 3mL sterile syringe and 26 gauge sterile needle (or equivalent cleared syringe and needle)
- UnoMedical Comfort Infusion Set (k051264) (or equivalent FDA-cleared infusion set)
- Power supplies with USB for charging the pump's internal battery
- Tandem Device Updater (TDU) software that allows remote updates of users' pumps

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. Persons with diabetes may also administer insulin by injection or by using other insulin infusion pumps as prescribed by his/her physician. 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 meet expectations and lifestyle.

There are similar insulin pumps, CGM systems and combined pump-CGM systems

currently on the market from this sponsor and other sponsors. 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 t:slim G4 System was approved for use in the United States on September 8, 2015. The device has not been withdrawn from the market for any reason related to its safety or effectiveness.

The t:slim X2 System is comprised of components (Sensor and Transmitter) of the FDA PMA-approved Dexcom G5 Mobile Continuous Glucose Monitoring System (P120005/S041 and P120005/S049) combined with the 510(k)-cleared Tandem t:slim Pump (k162080). Those devices have been marketed since their respective approval and clearance.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects associated with the use of the device.

Potential device-related serious events include:

- Hypoglycemia from over-delivery of insulin due to a pump defect or a CGM malfunction (e.g., failure to sense or display of incorrect glucose levels). Uncorrected, severe hypoglycemia can progress to seizure, unconsciousness, coma, and rarely, death. A user and/or parent should respond with glucagon, oral carbohydrates, and/or other medical assistance as indicated.
- Hyperglycemia and ketosis possibly leading to diabetic ketoacidosis (DKA) due to CGM malfunction (e.g., failure to sense or display of incorrect glucose levels) or a pump failure. Pump failures could include problems with the cannula, needle, insulin infusion set tubing, catheter occlusion, or dislodgement or fracture during infusion set insertion resulting in cessation of or decreased insulin delivery. A user and/or parent should respond with subcutaneous insulin and hydration, or other medical assistance, including intravenous insulin therapy, fluid, and electrolytes.
- Hypoglycemia or hyperglycemia related to other mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery.

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

- Skin irritation, redness, or rash.
- Infection at the sensor or insulin infusion sites.
- Pain or discomfort.
- Bruising.
- Edema.
- Rash.
- Bleeding.

- Induration of the skin.
- Allergic reaction to adhesives.
- Hyperglycemia as a result of inadequate or suspension of insulin delivery that is secondary to pump failure or problems with the cannula, needle, insulin infusion set tubing, and/or catheter occlusion, dislodgement or fracture during infusion set insertion. Ketosis and DKA if hyperglycemia persists for reasons listed above.
- Loss of communication between the pump and the sensor resulting in CGM values, alarms, and alerts not being available to the user.

Sensor breakage with fragments under the skin is a potential, but uncommon adverse event related to the CGM component of the t:slim X2 System. Based on postmarket experience with similar devices and results of other clinical studies, the occurrence and severity of these events do not raise major concerns.

The CGM component of the t:slim X2 System has lower overall accuracy than fingerstick blood glucose measurements and there are potential adverse effects 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. These inappropriate treatments could increase the risk of hypoglycemia or prolong hypoglycemia which can result in seizures, loss of consciousness, or rarely, death. Risks of falsely low readings include inappropriate administration of carbohydrate. These inappropriate treatments could increase the risks of hyperglycemia or prolong hyperglycemia, resulting in increased risks of acute or long term hyperglycemia-related complications and subsequent coma or death. 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, CGM instructions specifically advise users not to make large changes in insulin dosing based on the rate of change.

There are also potential adverse effects associated with the CGM 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 potential adverse effects associated with making acute and long-term therapy adjustments when information provided by the CGM 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.

For the specific adverse events that occurred in the clinical studies for the G4 Platinum CGM System, please refer to the SSED for P120005, P120005/S018, and P120005/S031.

IX. SUMMARY OF NONCLINICAL STUDIES

The t:slim X2 System hardware and software has been modified from the approved t:slim G4 System (P140015) to accommodate the Dexcom G5 Mobile CGM Sensor and Transmitter. Additionally, the Tandem Device Updater (TDU) software (originally cleared under k160482, k162080) used to remotely update the Pump has been modified to allow for compatibility with the Dexcom G5 Mobile System hardware. Testing in Section IX.A. addresses these modifications.

A. Laboratory Studies

See the SSED for P120005, P120005/S018, and P120005/S031 for pre-clinical testing that was referenced to support the Dexcom G5 CGM System.

The pre-clinical testing described below was performed on the t:slim X2 System. The changes in this submission were validated by performing appropriate software and hardware testing. Protocols, test reports, and acceptance criteria have been reviewed and found to be acceptable. Studies are described further in the following sections.

t:slim X2 System Testing

A pump drop test was conducted on the t:slim X2 pump. The drop testing procedure for the t:slim X2 pump was the same as the drop testing procedure for the t:slim G4 pump. The test met the acceptance criteria of at least 29 pumps passing the Functional Validation Test or failing safe.

Electrical safety was performed on the t:slim X2 System per IEC 60601-1, including compliance with the following collateral standards: IEC 60601-1-2, IEC 60601-1-8, IEC 60601-1-11, and IEC 60601-2-24.

Electromagnetic compatibility (EMC) testing was performed on the t:slim X2 System per IEC 60601-1-2, including the test level modifiers to the requirements as specified in IEC 60601-2-24. All EMC test levels, including those for immunity (e.g., radiofrequency (RF) radiated immunity, RF immunity, magnetic field immunity) and emissions (e.g., radiated emissions, conducted emissions), met or exceeded the requirements in these standards. Immunity essential performance criteria included no change of operating mode, no component failures, no changes in programmable parameters, and no reset to factory defaults. Additionally, immunity tests met the following acceptance criteria used in the testing:

- The pump does not over deliver a clinically significant amount of insulin to the patient.
- The pump does not under deliver a clinical significant amount of insulin without providing notification of this occurrence.
- The pump does not discontinue reporting data and status information from the glucose engine durng an active CGM session without providing notification.
- The displayed estimated glucose value (EGV) is not outside of the ± 5 mg/dL or ± 5% tolerance (whichever is greater) from the nominal EGV recorded for that test for more than one consecutive packet.

Electromagnetic interference from security and logistical systems (SLS) testing was conducted on the t:slim X2 System and all tests passed. Wireless coexistence testing was conducted on the t:slim X2 System and demonstrated that the device is safe in its intended environment.

For a description of prior pump and system testing, including Humalog and Novalog insulin compatibility and stability, insulin cartridge sterility, and insulin cartridge shelf life, see the SSED for P140015.

Biocompatibility Testing

See the SSED for P140015 for the description of biocompatibility testing.

Software Verification and Validation

Software modifications were made to the t:slim X2 System to accommodate the Dexcom G5 Mobile CGM Sensor and Transmitter. Comprehensive verification and validation testing was conducted to confirm that the software used in the t:slim X2 System met all specified requirements and performed as intended. Testing was carried out in accordance with FDA guidance "General Principles of Software Validation: Final Guidance for Industry and FDA Staff." Software development activities included establishing detailed software requirements, linking requirements with associated verification and validation activities, software code inspection, software code walkthrough, static code analysis, unit testing, and system level testing to ensure that the software conforms to patient needs and intended uses.

Modifications were made to the TDU software (originally cleared in k160482, k162080) to allow for compatibility with the Dexcom G5 Mobile System hardware. Comprehensive verification and validation testing was conducted to confirm that the TDU software met all specified requirements and performed as intended.

Human Factors Testing

For the expansion of the indication to include pediatric subjects ages 6-11 years in this submission, a Human Factors validation test was conducted to demonstrate that the t:slim G4 System was safe and effective for users ages 6-11 years and/or their

parent/guardian. This involved a simulated use test in which 33 representative pediatric users were asked to operate the device in a simulated use environment. The study participants received training that matched the training that patients would receive with the commercialized system. Critical tasks and critical comprehension tasks were identified and implemented, and objective and subjective data was collected and analyzed. The results of the study demonstrated that any residual risk remaining after the validation test would not be further reduced by modifications of design to the user interface and is outweighed by the benefits of the device.

The hardware and software changes in this submission did not require any changes to the user interface. Therefore, no additional human factors testing was conducted as a result of these hardware and software changes.

See the SSED for P140015 for a description of the human factors testing with the t:slim G4 System with users 12 years of age and greater.

Performance Qualification

There were no changes to the manufacturing process, including the pump refurbishment program (P140015/S009) and pump replacement program (P140015/S006), for the t:slim X2 System from the manufacturing process previously approved in P140015 supplements and annual report.

The t:slim X2 pumps underwent the same testing as the t:slim G4 pumps and included the following tests, which demonstrated acceptable results:

- The Drive Train Force Test: an in-process test used in production to measure the output force of the rack pushrod which is driven by the motor gearbox assembly. The rack pushrod is the point of engagement with the cartridge to drive insulin fill and dispense.
- The Automated Charge Cycle Test: a test that verifies the battery is working correctly.
- The Leak Test: a test that verifies the pump seals.
- The HiPot Test: a test that verifies the adequacy of electrical isolation.
- The Backlash Calibration Test: a test that determines the pump backlash and stores that value in the pump during production. Backlash is defined as a clearance between mating gear teeth.
- The Accelerated Basal Test: simulates approximately 30 days of pump use by pumping fluid through a recirculating cartridge at basal rate set by the test software.
- The Final Functional Test: tests all major sub-systems of the device.

The refurbished t:slim X2 pumps underwent the same testing as the refurbished t:slim G4 pumps and included the same tests described above (The Drive Train Force Test, The Automated Charge Cycle Test, The Leak Test, The HiPot Test, The Backlash Calibration Test, The Accelerated Basal Test Software, and The Final Functional Test). The test results were acceptable.

Packaging Integrity and Shipping Testing

No process changes were made to the packaging process. See the SSED for P140015 for testing information.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

The current supplement was submitted to expand the indication to include pediatric patients ages 6-11 years and change the indication from adjunctive to non-adjunctive CGM use (i.e., replace fingerstick blood glucose testing for diabetes treatment decisions). The class II Tandem t:slim Insulin Delivery System, which has the same intended use and technological characteristics as the t:slim X2 pump, is cleared for individuals 6 years of age and greater (k160056, k162080). The Dexcom G5 Mobile CGM System is approved for individuals 2 years of age and greater for non-adjunctive use (P120005/S041).

Dexcom performed clinical studies in both adult and pediatric subjects to establish a reasonable assurance of safety and effectiveness with the Dexcom G4 CGM System for detecting trends and tracking patterns in subjects with diabetes mellitus when used as an adjunct to blood glucose testing. See P120005/S018 and P120005/S031 for details on these clinical studies, including study design, patient accountability, and demographics including age ranges of subjects, safety and effectiveness results, and financial disclosure information. The clinical study to support P120005/S031 included pediatric patients and did not leverage existing data for adults to support the pediatric claim. The algorithm utilized in the Dexcom G4 CGM System was approved for use in the Dexcom G5 CGM System in P120005/S033. A retrospective analysis was conducted to verify and validate the change. The clinical study information in P120005/S018 and P120005/S031 was used to support a reasonable assurance of safety and effectiveness of the Dexcom G5 Mobile CGM System for replacement of fingerstick blood glucose monitoring for diabetes treatment decisions in the U.S (P120005/S041).

This submission leverages (by right of reference from Dexcom) the clinical studies performed in submissions P120005/S018 and P120005/S031. No new clinical study was conducted to support the change in the indications for the t:slim X2 System.

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

In accordance with the provisions of section 515(c)(3) 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, 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 P120005/S018 establish a reasonable assurance of safety and effectiveness with the Dexcom G4 Platinum CGM System for detecting trends and tracking patterns in adults with diabetes mellitus, adjunctively with blood glucose testing. The results of the clinical studies performed in P120005/S031 further support the use of this device for pediatric patients age 2 and older. These clinical studies were leveraged to support the performance of the Dexcom G5 CGM System (P120005/S033) and change in indication to replace fingerstick blood glucose monitoring for diabetes treatment decisions (P120005/S041). See the SSED for P120005/S018, P120005/S031, and P120005/S041 for additional information.

No additional clinical study was required for the t:slim X2 System. The preclinical data presented above (Section IX) as well as that described in P140015 establish a reasonable assurance of safety and effectiveness for the t:slim X2 System.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory data of the t:slim X2 System (described above in Section IX), data collected in clinical studies conducted to support PMA approval of the Dexcom CGM System (P120005/S018 and P120005/S031), and an FDA Advisory Committee meeting held for the change in indication from adjunctive to nonadjuntive use for Dexcom G5 Mobile CGM System (P120005/S041). Adverse events from P120005/S018 and P120005/S031 and the FDA Advisory Committee meeting from P120005/S041 are summarized below. Please also refer to potential adverse events in Section VIII above and benefit-risk determination in Section XII.C. below for additional information.

Several non-serious adverse events were reported for Dexcom G4 Platinum CGM System clinical studies. 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), thirteen 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.

An FDA Advisory Committee meeting was held on July 21, 2016 for the change in indication from adjunctive to nonadjuntive use for Dexcom G5 Mobile CGM System (P120005/S041). In public comments to the docket and comments made during the public comment period of the meeting, 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. Additionally, 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. The indication change was approved on December 20, 2016 and a subsequent confirmatory study of the device 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

Benefits

The benefits of this sensor augmented pump (SAP) are based on data collected in clinical studies and on the results of a former validation study that assessed the usability of the t:slim G4 in children and adolescents between the ages of 6 and 11.

Children and adolescents with diabetes demonstrate frequent glucose excursions and are particularly vulnerable to both hyperglycemia and hypoglycemia. The use of SMBG values to manage diabetes is well-established, but traditional SMBG provides only a snapshot of one glucose value at a specific time. The use of CGM in children and adolescents provides an additional level of protection against hyper- and hypoglycemia and facilitates a more comprehensive understanding of glucose trends and patterns in response to activities of daily living as well as typical childhood stressors such as illness, erratic eating habits, and variable physical activity levels.

Benefits of an insulin pump, including the t:slim insulin pump, include the ability to administer insulin in a manner that is more consistent with the normal physiologic release of insulin and that corresponds to individual needs and lifestyles. Both basal and bolus rates of insulin release incorporate factors such as insulin sensitivity, age, weight, usual activity, and typical diet and can be individualized to each child and adolescent to maximize insulin effectiveness. The integration of a CGM with an insulin pump (SAP) has the potential to assist children and adolescents, parents of young children incapable of or not quite independent enough for self-management and newly diagnosed children and adolescents in the detection and prevention of glucose excursions, particularly, hyperglycemia and hypoglycemia. The amount of information provided by the sensor can also be used to inform treatment decisions and improve glycemic control.

The probable benefits of the Dexcom G5 Mobile CGM System are based on data collected in the original PMA (P120005), P120005/S018, and P120005/S031

(described in the respective SSEDs) as well as reports of significant human experience with the CGM device provided by members of the public and discussions by the Clinical Chemistry and Toxicology Advisory Panel at the July 21, 2016 panel meeting described in the SSED for P120005/S041.

Non-adjunctive use of the Dexcom G5 Mobile CGM System can be expected to provide the benefit of decreased pain relative to fingerstick measurements and the Dexcom G5 Mobile CGM 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 Mobile CGM System relative to fingerstick glucose measurements can additionally have psychosocial benefit (e.g., reduced burnout and perceived stigma). Further, adherence to the recommended frequency of blood glucose self-monitoring is known to be suboptimal in many people with diabetes. The availability of non-adjunctive use of the Dexcom G5 Mobile CGM 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. 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.

Risks

Risks of the CGM include the following:

- The use of inaccurate glucose concentration data can result in an incorrect dose of insulin being delivered or suspended leading to hypo- or hyperglycemia.
- Young children may deliberately or inadvertently dislodge the sensor.
- Missed alerts, false negative and false positive alerts with corresponding treatment actions or lack thereof.
- Skin irritation or redness, inflammation, pain or discomfort, bruising, edema, rash, bleeding, infection, or allergic reaction due to either the sensor needle or the adhesive
- Sensor breakage leaving a sensor fragment under the skin

Risks of the pump include the following:

- Hypoglycemia from over-delivery of insulin due to a pump defect
- Cessation of or decreased insulin delivery resulting in hyperglycemia and possibly DKA due to pump failure, problems with the cannula or insulin infusion set tubing catheter occlusion, dislodgement, or fracture during infusion set insertion resulting in injury and/or inability to administer insulin
- Mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery
- Skin irritation, or redness, inflammation, pain or discomfort, bruising, edema, rash bleeding, infection, or allergic reaction at the infusion site

- Failure of the infusion set or complications at the infusion site, e.g. lipohypertrophy from repeatedly using the same site, resulting in inability to administer insulin or the variability of insulin absorption at the site.

Risks of the pump and CGM include both false positive and false negative readings with the following potential consequences:

False positive hyperglycemic readings:
- Inappropriate or excessive administration of insulin and failure to prevent or treat hypoglycemia.
- Loss of consciousness, seizures, or death related to severe or prolonged hypoglycemia.

False positive hypoglycemic readings:
- Failure to administer insulin or a sufficient amount of insulin to treat or prevent hyperglycemia.
- Failure to adjust insulin infusion increasing the risk of prolonging, inducing, or exacerbating hyperglycemia, including the risks of DKA or HHS.

False positive and negative high and low alerts and alarms:
- Needless increase in SMBG
- Disruption of patient activity or sleep.
- Alarm fatigue with subsequent deactivation of alarms & alerts
- Failure to recognize need to intervene with additional SMBG and indicated interventions.

False negative hypoglycemic readings:
- Failure to administer or insufficient administration of glucagon, carbohydrates or adjustment of insulin infusion.
- Inappropriate treatments could result in or prolong hypoglycemia and result in seizure, loss of consciousness, or death.

False negative hyperglycemic readings:
- Failure to recognize, prevent or treat hyperglycemia.
- Failure to adjust insulin infusion increasing the risk of prolonging, inducing, or exacerbating hyperglycemia, including the risks of DKA or HHS.

Other Factors

The overall accuracy of the Dexcom G5 Mobile CGM System 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 CGM 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 CGM 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 rely 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. Please refer to the SSED for P120005/S041 for more information.

Every insulin delivery method carries some degree of risk of a harmful event. However, health care providers (HCPs) generally will not prescribe insulin pumps to patients or parents/caregivers who do not demonstrate that they are checking glucose levels frequently (4-6 times/day), cannot recognize and treat the symptoms of both hypo- and hyperglycemia, and do not have some knowledge of “sick day rules”. Likewise, HCPs are not likely to prescribe sensors or sensor-augmented pumps to patients or parents/caregivers who are not engaged in care, demonstrate adequate self-management/management skills and willingness to perform finger stick blood glucose measurements twice daily for sensor calibration, and/or are seeking ways to improve glycemic control.

Children and adolescents often have high risk behaviors or developmental tasks, e.g. tampering with devices and acceptance by peers, respectively, which may interfere with self-management skills regardless of insulin delivery method. The use of an insulin pump, however, can be programmed with basal rates that can limit the severity of hyperglycemia, thus preventing DKA. Pre-set pump settings can also

insure that basal rates and bolus doses do not exceed the recommended TDD, thus reducing the risk of hypoglycemia. The t:slim X2 System has additional features such as screen lock out and lock screen 1,2, 3, which further mitigate the risk of inadvertent or modification of dosing amounts or rates. Therefore, although non-adherence to instructions and misuse of the pump or pump malfunction has the potential to result in hypo- or hyperglycemia, the pump has built in features that can mitigate these risks.

Additional safeguards which include pre-set pump settings, documentation of basal and bolus amounts of insulin delivered, placement of infusion sites and sensors in sites that are out of reach, adequately securing the infusion site and tubing can reduce the risk of deliberate or inadvertent tampering with device or insertion sites that may result in over or under-delivery of insulin in children or dislodgment of the tubing from the insertion site.

Pediatric participants and/or their parent/guardian demonstrated competency following training and were able to complete respective tasks, which were assigned in a safe and efficacious manner and were intended to mimic real-life use and events. Participants who experienced difficulty were able to recover from their use events either on their own or with help from their parent/guardian or the research moderator. Only patients/parents/caregivers that are willing to perform the necessary blood glucose checks, sensor changes and calibrations should be prescribed the system. Training should include verification that patients understand the principles and use of specific devices and provide satisfactory return demonstrations of manual tasks.

Risk mitigations associated with use of insulin pump therapy include labeling and training with a healthcare provider who has been certified as a pump/CGM trainer. Risk mitigations that would prevent children, especially young children, from altering basal and bolus rates include an auto-locking feature after setting basal rates and bolus doses and securing the infusion site and tubing and possibly beyond the reach of the child if so indicated. Users are also instructed to have a backup plan for therapy (e.g. insulin pen or syringe) in case they are unable to use their pump.

The sponsor revised the Owner's Booklet to reflect the changes made to extend the use of the Tandem t:slim X2 System to include patients between the ages of 6 and 11 years of age. They have determined that the language is consistent with an 8th grade reading level. The sponsor has included in the t:slim X2 User Guide a section entitled Important Pediatric User Information with the recommendations intended to help younger users and their parents/guardians program, manage and care for the System.

Patient Perspectives

A factor considered during the review of P120005/S041 in determining probable risks and benefits for the Dexcom G5 Mobile CGM System was the patient perspective. This included 85 individual public comments 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. Patients who provided public comment during this panel meeting 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. Please refer to the SSED for P120005/S041 for more information.

Conclusion

In conclusion, given the available information above, the data support that for the indications for use of the t:slim X2 System the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application (as well as previously approved premarket submissions) 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 t:slim X2 System outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on August 25, 2017.

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.

XV. REFERENCES

None.