

# 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

Device Trade Name: t:slim G4 Insulin Pump with Dexcom G4 Platinum CGM

Device Procode: MDS, OYC

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

Date of FDA Notice of Approval: September 8, 2015

Priority Review: *Not Applicable*

## II. INDICATIONS FOR USE

The t:slim G4™ Insulin Pump with Dexcom G4® Platinum CGM (“t:slim G4 System”) consists of the t:slim G4 Insulin Pump paired with the Dexcom G4 Platinum Sensor and Transmitter.

The t:slim G4 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 G4 Insulin Pump can be used solely for continuous insulin delivery and as part of the t:slim G4 System to receive and display continuous glucose measurements from the Dexcom G4 Platinum Sensor and Transmitter.

The t:slim G4 System also includes continuous glucose monitoring (CGM) indicated for detecting trends and tracking patterns in persons with diabetes for use as an adjunctive device to complement, not replace, information obtained from standard home glucose monitoring devices. The t:slim G4 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 G4 System results should be based on the trends and patterns seen with several sequential readings over time.

The t:slim G4 System is indicated for use in individuals 12 years of age and greater.

The t:slim G4 System is intended for single patient use and requires a prescription.

### III. **CONTRAINDICATIONS**

The t:slim G4 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

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

The t:slim G4 Pump, Dexcom G4 PLATINUM Transmitter, and Dexcom G4 PLATINUM 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 sensor glucose readings. The level of inaccuracy depends on the amount of acetaminophen active in the body and may be different for each person.

### IV. **WARNINGS AND PRECAUTIONS**

The warnings and precautions can be found in the t:slim G4 Insulin Pump with Dexcom G4 Platinum CGM System labeling.

### V. **DEVICE DESCRIPTION**

The t:slim G4 Insulin Pump with Dexcom G4 Platinum CGM, also referred to as the t:slim G4 System, consists of the t:slim G4 Insulin Pump paired with the Dexcom G4 Platinum Sensor and Transmitter. The G4 receiver functionality, including the radio and glucose signal processing algorithms, from the previously approved G4 Platinum CGM system (P120005) has been integrated into the insulin pump allowing the pump to receive CGM data from the G4 sensor and transmitter pair.

#### **The t:slim G4 Insulin Pump:**

The t:slim G4 Insulin Pump (“the pump”) is an ambulatory, battery operated, rate-programmable infusion pump designed for the continuous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. A custom 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 G4 Insulin Pump includes a color touch screen and incorporates various safety features to prevent the touchscreen from being inadvertently activated.

The t:slim G4 Insulin Pump includes a disposable insulin cartridge for storage of insulin. The cartridge attaches to the t:slim G4 Insulin Pump and is designed to hold up to 3 mL, or 300 units, of U-100 Humalog or NovoLog insulin. It is labeled as a single-use device and is intended to be replaced at least once every three days.

The t:slim G4 system contains a speaker and vibratory indicator used to annunciate 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 pump includes a non-user accessible, rechargeable lithium polymer battery. 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 G4 Platinum Sensor:**

The sensor used with the t:slim G4 system is identical to the sensor that was originally approved as part of the Dexcom G4 Platinum Continuous Glucose Monitoring System (P120005). The G4 Platinum Sensor (“the sensor”) is comprised of a sensor applicator, an adhesive pad, transmitter mount and the sensor probe. The G4 Platinum Sensor is a sterile, disposable device inserted by the user into the subcutaneous tissue using an applicator. The applicator is adhered to the surface of the skin with a standard medical grade adhesive pad. The applicator contains a 26-gauge introducer needle that contains the Sensor probe. The applicator inserts the wire under the user’s skin. After deployment the applicator is detached and disposed of by the user, exposing a transmitter mount (sensor pod) ready for placement of the G4 Platinum 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 G4 Platinum Transmitter:**

The transmitter that is intended to be used with the t:slim G4 system is identical to the transmitter that was originally approved as part of the Dexcom G4 Platinum Continuous Glucose Monitoring System (P120005), G4 Platinum Transmitter (“the 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 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 to the t:slim G4 Pump. The Transmitter collects the small electrical current from the Sensor and transmits the Sensor signal wirelessly at regular 5-minute intervals. A unique Transmitter ID must be entered into the t:slim G4 Pump to activate radiofrequency communication with the Transmitter, which allows the Sensor glucose readings to be displayed on the t:slim G4 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 6 months.

The System contains calibration and signal processing algorithms required to convert the Sensor's electrical signal to glucose values in mg/dL that can be displayed to the user. Calibrations for the CGM functionality of the System are performed twice daily by the patient using standard commercially-available blood glucose meter devices and entered manually by the patient into the t:slim G4 insulin pump. After calibrating the system, the pump automatically displays the current glucose value, trend graphs of recent glucose values and rate of change arrows once every five minutes.

The System provides audible or vibratory alerts for high and low glucose values. Dashed lines on the receiver screen indicate the current alert level settings. The user can configure the Pump to provide audible, vibratory or combined audible and vibratory alerts. The pump also contains a non-configurable low glucose alarm at 55 mg/dL to provide users additional warning of hypoglycemia. The fixed low alert at 55 mg/dL alerts users as a vibration first, followed by beeps 5 minutes later if not confirmed.

Dexcom G4 Platinum 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 G4 System. Thus, these components will be shipped under the Dexcom label and will not be explicitly labeled as part of the t:slim G4 System. The user guide for the t:slim G4 System will be provided with the t:slim G4 pump. That user guide explains how to combine the components.

In addition to the above described primary components of the device, the t:slim G4 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 an equivalent FDA-cleared infusion set ("infusion set")
- AC power supply with USB for charging the pump's internal battery (Wall and Car power USB adapters)
- t:connect/CGM Data Management Program, which is a web based software system that allows t:slim G4 system users, care givers and healthcare

professionals to view data retrieved from a t:slim G4 system and from various blood glucose meters.

## **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 has not been marketed in the United States or outside of the United States. As such, the device has not been withdrawn from marketing for any reason related to its safety or effectiveness.

The t:slim G4 System is comprised of components (Sensor and Transmitter) of the FDA PMA-approved Dexcom G4 Platinum Continuous Glucose Monitoring System (P120005) combined with the 510(k)-cleared Tandem t:slim Pump (k141758). 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 (e.g., complications) associated with the use of the device.

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

- Skin irritation, itching, scarring, redness or skin discoloration
- Infection
- Pain or discomfort

- Bruising
- Edema
- Rash
- Bleeding
- Allergic reaction to adhesives
- Hypoglycemia from over-delivery of insulin
- Hyperglycemia and ketosis possibly leading to ketoacidosis due to pump malfunction, or problems with the cannula, needle, or insulin infusion set tubing resulting in cessation of insulin delivery
- Loss of communication between the pump and the sensor resulting in CGM values, alarms, and alerts not being available to the user
- Catheter occlusion resulting in missed insulin dosing
- Catheter dislodgement or fracture during infusion set insertion resulting in injury and/or inability to administer insulin
- Failures of the infusion set or at infusion site resulting in inability to administer insulin
- Mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery

Sensor needle breakage during sensor insertion, wear or removal with fragments retained under the skin and catheter fracture during infusion set insertion are potential procedure-related complication. Based on post-market experience with similar devices and the results observed in this clinical study, the occurrence and severity of these events do not raise major concerns.

One potential risk of combining the CGM and the pump is that the user might be more inclined to use the CGM data in an unapproved way to determine their insulin dose. Inaccurate sensor results, if used to make dosing decisions, may lead to hypo- or hyperglycemia. However, no further complications are expected due to the pump being combined with the CGM as a system beyond the potential complications of the pump or CGM alone.

Like other insulin pumps, there is an inherent risk that patients who do not use the system as instructed (non-adherence) could harm themselves. Patients should be informed that sensor interstitial glucose values should not be used to make insulin dose decisions and that all threshold alerts and alarms should be confirmed with a blood glucose measurement.

The risks of actions taken based on false positive hyperglycemic readings include inappropriate or excessive administration of insulin and failure to treat hypoglycemia. These inappropriate treatments could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death. The risks of actions taken based on false positive hypoglycemic readings include failure to administer insulin and failure to treat hyperglycemia. False positive high alerts and low alerts and alarms may increase the number of unplanned blood glucose checks; and disrupt patient activity and sleep. If the

false positive rate is too high it can result in ‘alarm fatigue’ and patients may deactivate these alerts/alarms.

The risks of actions taken based on false negative hyperglycemic readings include failure to administer or insufficient administration of insulin and inappropriate administration of extra carbohydrate. These inappropriate treatments could prolong or induce hyperglycemia. The risks of actions taken based on false negative hypoglycemic readings include inappropriate administration of insulin or failure to administer or insufficient administration of extra carbohydrate. These inappropriate treatments could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death. False negative high alerts and low alerts and alarms will prevent the patient from having the opportunity to perform unplanned blood glucose tests and treat as instructed by their healthcare providers. There are additional possible risks if the system inaccurately calculates the rate of change of glucose.

The CGM component is to be used only for tracking and trending glucose levels. The risk related to either an inaccurate sensor value outside of the patient’s normal range or a false alert or alarm is the risk of performing an unnecessary additional blood glucose test to confirm the erroneous sensor reading. The risk of medical harm may be mitigated through labeling which emphasizes that patients should confirm all CGM readings prior to making treatment decisions.

The risks of the device failing to alert an asymptomatic user to a high or low blood sugar is no greater than that associated with traditional blood glucose monitoring.

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

## **IX. SUMMARY OF PRECLINICAL STUDIES**

A summary of the non-clinical laboratory studies that were performed on the t:slim G4 Insulin System are summarized below. See the SSED for P120005 for additional pre-clinical testing performed on the Dexcom G4 Platinum CGM System.

### **A. Laboratory Studies**

The nonclinical studies focused on bench testing to support compliance with component and system requirement specifications and testing of hardware requirements, insulin cartridge requirements and mechanical requirements. Additionally, system level testing (Performance, Environmental/Operational, and System Level Packaging/Shipping) was completed. Protocols, test reports and acceptance criteria have been reviewed and found to be acceptable.

**Table 1: T:slim G4 System Testing**

<b>Test</b>	<b>Purpose</b>	<b>Acceptance Criteria</b>	<b>Results</b>
Pump Environmental Storage -20°C to 60°C with 20 % and 90% relative humidity	Demonstrate reliable operation of t:slim G4 pumps after storage environmental conditions	All units must pass the final functional tests including USB communication, LED, Display, vibrate motor, drive motor, speaker operation and battery operation.	PASS
Pump Simulated Shipping per ASTM D4169	Demonstrate reliable operation of t:slim G4 pumps after shipping conditions	All units must pass the final functional tests including USB communication, LED, Display, vibrate motor, drive motor, speaker operation and battery operation after initial manual handling, vehicle stacking, loose load vibration, vehicle vibration, concentrated impacts and final manual handling.	PASS
Drop Resistance at height of 1 meter on each of the 4 corners and 6 faces on to 50 mm thick hardwood per IEC 60601-1 3rd ed 15.3.4.1	Demonstrate compliance to product specification regarding drop resistance	At least 29 pumps pass Functional Validation Test. All units must have no signs of a hazardous condition.	PASS
Fluid Ingress per IPX7	Demonstrate reliable operation of t:slim G4 pumps when exposed to water	All units must pass the final functional tests including USB communication, LED, Display, vibrate motor, drive motor, speaker operation and battery operation after immersion to 3 ft for 30 minutes.	PASS
Battery Verification	Verify rated battery life after 4 years of simulated depletion and recharging conditions	All units must meet rated battery life of 5 days of typical usage between recharging after 4 years of simulated depletion and recharging.	PASS

Test	Purpose	Acceptance Criteria	Results
Random Vibration test per IEC 60601-1-11	Demonstrate reliable operation of t:slim G4 pumps under home use vibration conditions	All units must pass the final functional tests including USB communication, LED, Display, vibrate motor, drive motor, speaker operation and battery operation after exposure to broad band random vibration 10 to 100 Hz 1.0 (m/s <sup>2</sup> ) <sup>2</sup> /Hz, 100 Hz to 200 Hz -3dBper octave, 200 Hz to 2,000 Hz, 0.5 (m/s <sup>2</sup> ) <sup>2</sup> /Hz 30 min for perpendicular axis (3 total).	PASS
Mechanical Shock per IEC 60601-1-11	Demonstrate reliable operation of t:slim G4 pumps under home use mechanical shock conditions	All units must pass the final functional tests including USB communication, LED, Display, vibrate motor, drive motor, speaker operation and battery operation after exposure to mechanical shock per IEC 60068-2-31 procedure 1.	PASS
Vibrator Motor Testing	Demonstrate vibrator motor functions per specifications	Vibrator motor must activate when commanded. Vibration must be physically felt in hand when activated.	PASS
Cartridge Push Test	Demonstrate compliance to product specification regarding push test	No damage to the Luer connection or cartridge bore that allows the free flow of fluid. The flow of water with 1 psig of pressure applied to the cartridge shall be less than 0.1 Units/hr/psiG (1.0 mm <sup>3</sup> /Hr/psiG).	PASS
Wake button cycling	Demonstrate reliable operation of t:slim G4 pumps after 4 years of simulated use	All units must pass the final functional tests including USB communication, LED, Display, vibrate motor, drive motor, speaker operation and battery operation after 4 years of simulated use of the	PASS

<b>Test</b>	<b>Purpose</b>	<b>Acceptance Criteria</b>	<b>Results</b>
		wake button.	
Motor Gear box cycling	Demonstrate reliable operation of t:slim G4 pumps after 4 years of simulated use	All units must pass the final functional tests including USB communication, LED, Display, vibrate motor, drive motor, speaker operation and battery operation after 4 years of simulated use of the motor and gear box assembly.	PASS
Occlusion Detection Test	Demonstrate ability of system to detect the presence of an occlusion and notify the user at minimum basal rate, intermediate basal rate and bolus.	Meets detection times of less than 2 hours at the intermediate rate and < 36 hrs at the minimum basal flow rate and less than 3 minutes during bolus delivery.	PASS
Delivery Volume Accuracy	Demonstrate accuracy of pumps to deliver minimum basal rate, intermediate basal rate, minimum bolus and large bolus.	Meets delivery accuracy of $\pm 5\%$ overall mean percentage error using methods of IEC 60601-2-24 for minimum basal rate, intermediate basal rate and bolus delivery.	PASS
Bolus Delivery Time	Demonstrate compliance to product specification regarding bolus delivery rate.	Data inspected to confirm no anomalous behavior.	PASS
Cartridge Detection	Demonstrate compliance to product specification regarding cartridge detection time.	During the delivery of a standard bolus, removal of the cartridge detected within 20 seconds. During basal delivery, removal of cartridge detected within 0.75 units.	PASS
Cartridge Volume	Demonstrate the compliance to insulin volume estimation requirements	The device provides an estimate for the remaining insulin volume, the calculation for which is to always be conservative.	PASS

<b>Test</b>	<b>Purpose</b>	<b>Acceptance Criteria</b>	<b>Results</b>
Self Priming	Demonstrate self-priming capability.	The system shall capable of self-priming	PASS
Pump-Infusion Site Height Differential	Demonstrate that unintentional flow does not occur due to 90cm infusion site height differential	Demonstrate flow accuracy of $\pm 25\%$	PASS
Pump Operating temperature	Demonstrate delivery accuracy over range of operating temperatures	Meets delivery accuracy of $\pm 5\%$ overall mean percentage error using methods of IEC 60601-2-24 for intermediate basal rate.	PASS
Pump Operating Pressure	Demonstrate delivery accuracy over range of operating pressures	Meets delivery accuracy of $\pm 15\%$ overall mean percentage error using methods of IEC 60601-2-24 for intermediate basal rate for pressures between Dead sea level and 10,000 feet per IEC 60601-1-11.	PASS
Alarm Pressure Level Test	Demonstrate ability of pump to generate auditory alarms which meet the standard of IEC 60601-2-24	Greater than 45 dBA at 1m	PASS
EMC/EMI Testing	Demonstrate ability of pump to operate in environments with EMI which meet the standard of EN 60601-1-2:2007	Maintain insulin delivery accuracy, maintain CGM functionality, estimated glucose value remains within $\pm 5\text{mg/dL}$ or 5%, whichever is greater	PASS
ESD Compliance	Demonstrate ability of pump to withstand expected levels of ESD which meet the standard of IEC61000-4-2	Maintain insulin delivery accuracy, maintain CGM functionality, estimated glucose value remains within $\pm 5\text{mg/dL}$ or 5%, whichever is greater	PASS
Wireless Coexistence	Demonstrate ability of device to withstand expected levels of wireless transmission	Continue to operate without impact on performance or function	PASS

Test	Purpose	Acceptance Criteria	Results
	from other sources		
FCC	Demonstrate compatibility with FCC regulation	The wireless radio, as utilized, is designed only to receive information, and is exempt from the need for FCC approval	PASS
Operational Range (distance)	Demonstrate compliance with product specifications regarding operational range.	Confirm that the radio reliably receives communication from an external wireless continuous glucose monitoring transmitter and sensor at a minimum range of 20 feet in open air.	PASS
Communication with CGM	Demonstrate ability to communicate with a paired CGM device	Confirm that the pump is capable of pairing with and displaying information from a CGM device	PASS
Pump and CGM History	Demonstrate compliance with product specifications regarding data logging and history	Confirm data logging functionality which can support up to 30 days of Pump and CGM history logging including date, time, amount and type (BG, carb, unit) of boluses, readings from SMBG meter, and estimated glucose values received from CGM	PASS
Cleaning Capability	Demonstrate reliable operation of t:slim G4 pumps after external cleaning.	All units must pass the final functional tests including USB communication, LED, Display, vibrate motor, drive motor, speaker operation and battery operation with no visible damage after external cleaning.	PASS
USB Door & Connector Cycling	Demonstrate reliable operation of USB door of t:slim G4 pumps after 4 years of simulated use.	All units must pass the final functional tests including USB communication, LED, Display, vibrate motor, drive motor, speaker operation and battery operation after 4	PASS

Test	Purpose	Acceptance Criteria	Results
		years of simulated use of the USB Door and Connector	
Cartridge Installation Cycling	Demonstrate reliable operation of t:slim G4 pumps after 4 years of simulated use.	All units must pass the final functional tests including USB communication, LED, Display, vibrate motor, drive motor, speaker operation and battery operation after 4 years of simulated use of the Pump Housing.	PASS

### Biocompatibility Testing

The t:slim G4 insulin cartridge was tested for biocompatibility in accordance with International Standard ISO-10993-1 as an external communication device with a duration of patient tissue contact of greater than twenty four hours to thirty days (category B). The table below (Table 2) summarizes the biocompatibility testing conducted on cartridge. Biocompatibility testing of the t:slim G4 Sensor and Transmitter were conducted in PMA P120005.

**Table 2: Insulin Cartridge Biocompatibility Testing Summary**

Test	Result
Cytotoxicity (MEM Elution)	Non-toxic
Sensitization	No evidence of sensitization
Irritation or Intracutaneous Reactivity	Non-irritant
Systemic Toxicity (Acute)	Non-toxic
Hemocompatibility	Non-hemolytic
Subacute/ Subchronic Toxicity	Negative
Implantation	Non-irritant
Genotoxicity (Ames Test)	Non-mutagenic
Genotoxicity (Chromosome Aberration)	Non-genotoxic
Genotoxicity (Mouse Micronucleus)	Non-mutagenic

### Electrical Safety and Electromagnetic Compatibility and Interference Testing:

Electromagnetic compatibility (EMC) and electromagnetic immunity (EMI) testing was performed for the t:slim G4 Insulin Pump per IEC 60601-1-2. All tests met the following acceptance criteria used in the testing:

- The system does not over deliver a clinically significant amount of insulin to patient.
- The system does not under deliver a clinically significant amount of insulin without notification.
- The system does not deliver a clinically significant amount of insulin to the patient after an occlusion.
- The pump shall not discontinue reporting data and/or information from the glucose engine to the user without notification.

Radiofrequency (RF) communication testing was performed on the t:slim G4 System demonstrating compliance with Federal Communications Commission standards (Title 47 Part 15). Radiated Emissions Test, Occupied Bandwidth, and Band-edge Measurement testing was performed. All tests passed.

Radiofrequency wireless testing was conducted on the t:slim G4 System, including wireless co-existence. Testing demonstrated that the System can operate in the presence of RF interference and co-exists with other wireless devices operating in the same vicinity. The communication distance of 20 feet between the Dexcom G4 Platinum Transmitter and the t:slim G4 insulin pump was verified. All tests passed.

Electrical safety testing was performed per IEC 60601-1, including compliance with the following collateral standards: IEC 60601-1-2, IEC 60601-1-8, IEC 60601-1-11, IEC 60601-2-24.

#### Insulin Compatibility and Stability:

In vitro testing was performed to assess extractables and leachables and insulin compatibility with the insulin drugs Humalog and Novolog and the insulin cartridge. To support the compatibility of the insulin analogs with the 3 mL disposable cartridge the stability of Humalog and Novolog were evaluated and support the compatibility of the insulin analogs in the cartridge for 6 days at 25°C and under stressed, worst-case conditions up to 3 days at 37°C. The studies also observed acceptable results of, degradation products and extractables and leachables.

#### Insulin Cartridge Sterility:

A gamma sterilization process is used to sterilize the t:slim G4 disposable insulin cartridge sealed in a Tyvek/polyethylene pouch according to the requirements of ISO 11137-1. Results from sterilization studies demonstrate that the gamma sterilization process for the t:slim G4 insulin cartridge consistently achieve a SAL of  $10^{-6}$ . Sterility of the Dexcom CGM system components (applicator, transmitter housing/base, insertion needle, Sensor) were provided under P120005.

#### Insulin Cartridge Shelf Life:

The shelf life of the 3 mL insulin cartridge has been established as 24 months from the date of sterilization when stored at -4°F to 140°F (-20°C to 60°C) and 20% to 90% relative humidity.

Packaging Integrity and Shipping Testing:

The t:slim G4 Insulin Pump was tested under conditions of simulated shipping per ASTM D4169. Testing included visual inspection, bubble testing, leak testing, peel testing, and visual labeling inspection. The tests demonstrated that the tested pumps passed after exposure to simulated shipping conditions.

The insulin cartridges can be packaged in 2- pack or 10-pack boxes. Testing to support these packaging configurations included accelerated aging, distribution simulation, visual inspection, simulated shipping, seal strength testing, microbial ranking, and bubble leak testing.

Software Verification and Validation:

Comprehensive verification and validation testing was conducted to confirm that the software used in the t:slim G4 System meets all specified requirements and that the software will operate reliably and safely under normal or abnormal use conditions.

The software verification and validation were carried out in accordance with the FDA's "General Principles of Software Validation: Final Guidance for Industry and FDA Staff." Software development activities included establishing detailed software requirements, linking requirements with associate verification tests, software code reviews, unit testing, system level testing and defect tracking and dispositioning to ensure the software conforms to patient needs and intended uses.

Human Factors Testing:

Formative and summative human factors studies were conducted with the stand alone t:slim G4 insulin pump as well as the t:slim G4 System. The summative study was a non-randomized, multicenter study that was performed using the t:slim G4 System and 30 representative participants interacting with the device in a simulated use environment. The study participants received training that was consistent with the training that patients would receive with the commercial product. Usability evaluations were performed that included critical device tasks and results of the study demonstrated that the potential benefits of the device outweighed the risks.

**B. Animal Studies**

No animal studies were conducted using the t:slim G4 System.

**C. Additional Studies**

None

**X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)**

Dexcom performed a clinical study to establish a reasonable assurance of safety and effectiveness with the Dexcom G4 Platinum CGM System for detecting trends and tracking patterns when used as an adjunct to blood glucose testing in subjects with diabetes mellitus. Please see the original P120005 SSED for details on this clinical study, including Financial Disclosure information.

No additional clinical study was conducted using the t:slim G4 System.

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

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

**XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES**

**A. Effectiveness Conclusions**

The results of the pivotal clinical study performed in P120005 establish a reasonable assurance of safety and effectiveness with the Dexcom G4 Platinum CGM System for detecting trends and tracking patterns when used as intended, as an adjuvant to blood glucose testing in subjects with diabetes mellitus. See P120005 SSED for additional information.

No additional clinical study was required for the t:slim G4 System. The preclinical test data presented above (Section IX) establish a reasonable assurance of safety and effectiveness for the t:slim G4 System. The results of the pre-clinical testing demonstrate that the t:slim G4 System complies with the applicable voluntary standards for biocompatibility, sterilization, Electromagnetic Compatibility and Safety. The device passed all the testing in accordance with national and international standards. Internal verification and validation testing confirmed that product specifications were met which support the intended use and technological characteristics. The verification and validation of the device software were completed according to the FDA guidance entitled General Principles of Software Validation: Final Guidance for Industry and FDA Staff.

The clinical testing performed in P120005 for the Dexcom G4 Platinum CGM System and the non-clinical and human factors/usability testing completed on the t:slim

System and its components for this PMA support the operation of this device as a system.

## **B. Safety Conclusions**

The risks of the device are based on nonclinical laboratory data of the t:slim G4 System (as described above) as well as data collected in a clinical study conducted to support PMA approval of the Dexcom G4 Platinum CGM System as described in the SSED for P120005.

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

- Skin irritation or redness
- Infection
- Pain or discomfort
- Bruising
- Edema
- Rash
- Bleeding
- Allergic reaction to adhesives
- Hypoglycemia from over-delivery of insulin
- Hyperglycemia and ketosis possibly leading to ketoacidosis due to pump malfunction, or problems with the cannula, needle, or insulin infusion set tubing resulting in cessation of insulin delivery
- Loss of communication between the pump and the sensor resulting in CGM values, alarms, and alerts not being available to the user
- Catheter occlusion resulting in missed insulin dosing
- Catheter dislodgement or fracture during infusion set insertion resulting in injury and/or inability to administer insulin
- Failures of the infusion set or at infusion site resulting in inability to administer insulin
- Mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery.

Sensor breakage with fragments retained under the skin and catheter fracture during infusion set insertion are potential procedure-related complication. Based on post-market experience with similar devices and the results observed in this clinical study, the occurrence and severity of these events do not raise major concerns.

One potential risk of combining the CGM and the pump is that the user might be more inclined to use the CGM data in an unapproved way to determine their insulin dose. This can result in an incorrect dose of insulin being delivered leading to hypo or hyperglycemia as the CGM sensor has not been approved to be used to dose insulin. However, no further complications are expected due to the pump being combined with the CGM as a system beyond the potential complications of the pump or CGM alone.

A pump malfunction could lead to clinically significant hypoglycemic event, ketosis or ketoacidosis. A patient should respond with carbohydrate, insulin therapy, hydration, or other medical assistance as necessary. If unaddressed, severe hypoglycemia, severe hyperglycemia and ketoacidosis can result in serious harm and death.

The user might be more inclined to use the CGM data in an unapproved way to determine their insulin dose. This can result in an incorrect dose of insulin being delivered leading to hypo or hyperglycemia as the CGM sensor has not been approved to be used to dose insulin.

Risks of actions taken based on false positive hyperglycemic readings include inappropriate or excessive administration of insulin and failure to treat hypoglycemia which could in or prolong hypoglycemia and result in seizures, loss of consciousness, or rarely, death. False positive high alerts and low alerts and alarms could increase the number of unplanned blood glucose checks; and disrupt patient activity and sleep. If the false positive rate is too high it can result in ‘alarm fatigue’ and patients may deactivate these alerts/alarms. Risks of actions taken based on false negative hypoglycemic readings include inappropriate administration of insulin or failure to administer or insufficient administration of extra carbohydrate which could result in or prolong hypoglycemia and result in seizures, loss of consciousness, or death. False negative high alerts and low alerts and alarms will prevent the patient from having the opportunity to perform unplanned blood glucose tests and treat as instructed by their healthcare providers.

The CGM component is to be used only for tracking and trending. The risk related to either an inaccurate sensor value outside of the patient’s normal range or a false alert or alarm is the risk of performing an unnecessary additional blood glucose test to confirm the erroneous sensor reading. The risk of medical harm may be mitigated through labeling which emphasizes that patients should confirm all CGM readings prior to making treatment decisions.

These risks are similar to the risks associated with the separate components.

### **C. Benefit-Risk Conclusions**

The probable benefits of the device are based on data collected in clinical and nonclinical studies conducted to support PMA approval as described above and in P120005.

Additional factors to be considered in determining probable risks and benefits for the t:slim G4 System included the following.

The CGM component of this system is intended to supplement self-monitoring of blood glucose to track and trend interstitial glucose levels as estimates of glucose excursions in the blood. The system provides continuous measurements of glucose in the tissue every 5 minutes for up to seven days for each sensor. Glucose trends and

the hypoglycemia and hyperglycemia alerts are intended to warn patients that they need to test their blood sugar to see if they need to take action to treat or prevent a hypoglycemic or hyperglycemic event. Other benefits of the CGM component include the following:

- Provide information regarding patterns of glycemic excursions throughout the day and night when patients may be unable to test their blood glucose
- The alert/alarm functions aid in the early detection of episodes of hyperglycemia and hypoglycemia (which may facilitate both acute and long-term therapy adjustments that may minimize episodes of hyper and hypoglycemia)
- Timely estimation of both point blood glucose concentration and rate of change in blood in addition to providing tracking and trending of glucose patterns both in the short term and over several days by this device. This information will aid in the prevention of extremes of glycemia.
- The results from this device will provide more detailed information regarding patterns of glycemic trends than is possible with traditional self-blood glucose testing with meters and that this information, combined with traditional glucose monitoring, will aid in the management of diabetes.

The insulin pump component of the system is indicated for continuous subcutaneous insulin infusion for the management of insulin-requiring diabetes. The pump is intended to assist patients in the management of their diabetes by allowing for various basal and bolus delivery settings. Other benefits of the pump component include the following:

- Ability to administer insulin frequently without repeated injection
- Ability to set different basal rates through the day to better match basal insulin requirements which may fluctuate during the course of the day
- Ability to calculate active insulin remaining from previous boluses to avoid “insulin stacking”, which can lead to hypoglycemia
- Ability to administer bolus doses over an extended time
- Ability for patient to calculate appropriate bolus insulin doses based on their individual needs

The functions of the sensor augmented pump are not feasible using traditional blood glucose monitoring and insulin self-injections as blood glucose meters only provide information about discrete, intermittent blood glucose levels and therefore are unable to provide information regarding patterns of glycemic excursions throughout the day and night when patients may be unable to test their blood glucose.

Other benefits of the system include the following:

- Single user interface
- Convenience to user – one less device to carry
- Improved user experience

The integration of the CGM and insulin pump functionalities is expected to improve patients’ experience with the device and may further improve glycemic control over the use of the pump alone or the CGM alone.

Risks of the pump include the following:

- Hypoglycemia from over-delivery of insulin due to a pump defect
- Hyperglycemia and ketosis possibly leading to ketoacidosis due to inappropriate pump failure or problems with the cannula, needle, or insulin infusion set tubing, resulting in cessation of or decreased insulin delivery
- Catheter 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
- Catheter occlusion resulting in missed insulin dosing
- 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 at the infusion site resulting in inability to administer insulin

Risks of the system include the following:

- Loss of communication between the pump and the sensor resulting in CGM values not being available to the user
- Use of inaccurate sensor values to make dosing decisions, resulting in an incorrect dose of insulin being delivered leading to hypo or hyperglycemia and their subsequent complications

These risks are similar to the risks associated with the separate components.

The previously approved CGM (P120005) has been integrated with the insulin pump so the information (results, alerts, alarms, etc.) for the pump and the CGM are displayed on the pump screen.

The benefits of the t:slim G4 System include the benefits of each of the pump and the CGM, and the additional benefits of a single user interface and the convenience to the user of not having to carry both a pump and the CGM receiver. There are no benefits lost through integration of the two devices into a single system. The risks of the t:slim G4 System include the risks of the pump and the CGM as well as the potential for loss of communication between the pump and the CGM and the use of inaccurate sensor values to make dosing decisions. These additional risks are similar to risks associated with the CGM, where communication between the sensor and receiver may be lost and users may use inaccurate sensor values to make dosing decisions. For risks associated with the t:slim G4 System (including pump and CGM specific risks), risk mitigations include design, labeling, and patient training. The benefits of the CGM outweigh its risks and the benefits of the pump outweigh its risks. Similarly, for the t:slim G4 System, the benefits of the combined system outweigh the risks.

In conclusion, given the available information above, the data support that for continuous subcutaneous insulin infusion for the management of insulin-requiring

diabetes and for detecting trends and tracking patterns in glucose levels, the probable benefits outweigh the probable risks.

**D. Overall Conclusions**

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The benefits of using the t:slim G4 System, as discussed above, outweigh the risks.

**XIII. CDRH DECISION**

CDRH issued an approval order on September 8, 2015. The final conditions of approval cited in the approval order are described below.

The applicant's manufacturing facility(ies) has/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.