SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Automated Insulin Dosing, Threshold Suspend; Non-adjunctive Invasive Glucose Sensor
Device Trade Name:	t:slim X2 Insulin Pump with Basal-IQ Technology
Device Procode:	OZO, 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: P180008

Date of FDA Notice of Approval: June 21, 2018

II. INDICATIONS FOR USE

The t:slim X2 Insulin Pump with Basal-IQ Technology (the System) consists of the t:slim X2 Insulin Pump which contains the Basal-IQ technology, and a continuous glucose monitor (CGM). Compatible CGMs include the Dexcom G5 Mobile CGM and integrated continuous glucose monitors (iCGMs) that are listed in the labeling for this device.

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 Insulin Pump with Basal-IQ Technology System.

When the System is used with the Dexcom G5 Mobile CGM or a compatible iCGM, the Basal-IQ Technology can be used to suspend insulin delivery based on CGM sensor readings.

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

The System is indicated for use in individuals 6 years of age and greater.
The System is intended for single patient use and requires a prescription.
The System 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 Insulin Pump with Basal-IQ 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 Insulin Pump with Basal-IQ, 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 Basal-IQ and Dexcom G5 Mobile CGM labeling.

V.   **DEVICE DESCRIPTION**

The t:slim X2 Insulin Pump with Basal-IQ consists of the t:slim X2 Insulin Pump paired with the Dexcom G5 Mobile sensor and transmitter. The Dexcom G5 Mobile Sensor and Transmitter work together to wirelessly send glucose readings to the t:slim X2 Insulin Pump with Basal-IQ. The t:slim X2 Insulin Pump with Basal-IQ was modified from the approved t:slim X2 Insulin Pump (P140015/S020) to include a Predictive Low Glucose Suspend (PLGS) feature (referred to as "Basal-IQ" Technology) that allows users to automatically suspend delivery of insulin when the predicted glucose value falls below a predefined, threshold value.

Tandem Diabetes Care, Inc. has received a right of reference from Dexcom to leverage the data in P120005, P120005/S018, P120005/S031, P120005/S033, P120005/S041, and P120005/S049 to support use of the Dexcom G5 Mobile CGM with the t:slim X2 Insulin Pump with Basal-IQ. See the SSEDs for P120005, P120005/S018, P120005/S031, and P120005/S041for additional information.

<u>t:slim X2 Insulin Pump with Basal-IQ</u>

The t:slim X2 Insulin Pump with Basal-IQ 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 with Basal-IQ 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 with Basal-IQ includes a disposable insulin cartridge for storage of insulin. The cartridge attaches to the t:slim X2 Insulin Pump with Basal-IQ 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 Insulin Pump with Basal-IQ 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.

The insulin pump software contains a Predictive Low Glucose Suspend (PLGS) algorithm (referred to as "Basal-IQ" technology) that assesses glucose information provided by the CGM and temporarily suspends insulin delivery in cases of impending or detected low blood glucose. Every 5 minutes, the Basal-IQ feature assesses glucose information provided by the CGM to predict whether glucose values will fall below 80 mg/dL in the next 30 minutes or detect if glucose levels are currently below 70 mg/dL. Under these conditions it will suspend insulin delivery; otherwise insulin delivery continues as normal. After insulin delivery is suspended, delivery resumes when the system detects glucose values begin to rise. A sustained suspension period when blood glucose is above the sensor suspend threshold is mitigated by a maximum suspend time where the Basal-IQ will resume insulin delivery after 120 minutes of suspension within a 150 minute window.

The t:slim X2 Insulin Pump with Basal-IQ can receive interstitial sensor glucose values from the Dexcom G5 Mobile CGM, or from a compatible iCGM system (cleared under 21 CFR 862.1355), via Bluetooth Low Energy (BLE) communication. Compatible iCGM systems are cleared and marketed separately from the t:slim X2 Insulin Pump with Basal-IQ system.

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 with Basal-IQ. The Transmitter collects the small electrical current from the Sensor and transmits the Sensor signal wirelessly to the t:slim X2 Insulin Pump with Basal-IQ at regular 5-minute intervals. A unique Transmitter ID must be entered into the t:slim X2 Pump with Basal-IQ to activate radiofrequency communication with the Transmitter, which allows the Sensor glucose readings to be displayed on the t:slim X2 Insulin Pump with Basal-IQ 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 Insulin Pump with Basal-IQ. The user guide for the t:slim X2 Insulin Pump with Basal-IQ will be provided separately and will explain how to combine the t:slim X2 Insulin Pump with Basal-IQ to Dexcom's CGM.

Other Compatible Devices

In addition to the above described primary components of the device, the t:slim X2 Insulin Pump with Basal-IQ can be used with the additional devices listed below:
- Compatible iCGM systems (regulated under 21 CFR 862.1355) listed in the t:slim X2 Insulin Pump with Basal-IQ labeling
- 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

A prior version of this insulin pump, the t:slim G4 Insulin Pump with Dexcom G4 Platinum CGM ("t:slim G4 System) was approved for use in the United States on September 8, 2015 (approved in P140015). The device has not been withdrawn from the market for any reason related to its safety or effectiveness.

The t:slim X2 Insulin Pump was modified from the approved t:slim G4 System (P140015) to include the functionality of the approved Dexcom G5 CGM System in P140015/S020. The t:slim X2 System (approved in P140015/S020 on August 25, 2017) is comprised of components (Sensor and Transmitter) of the FDA PMA-approved

Dexcom G5 Mobile Continuous Glucose Monitoring System (P120005, P120005/S018, P120005/S031, P120005/S033, P120005/S041, P120005/S049) combined with the 510(k)-cleared Tandem t:slim Pump (k162080). Those devices have been marketed since their respective approvals and clearance and have not been withdrawn from the market for any reason related to its safety or effectiveness.

VIII. <u>POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH</u>

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.

- Dysglycemia as a result of inappropriate suspension or resumption of insulin delivery due to inaccurate Basal-IQ function.

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.

Potential CGM-related complications:

- Sensor breakage with fragments under the skin is a potential, but uncommon adverse event related to the CGM. 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 with Basal-IQ 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 G5 Platinum CGM System, please refer to the SSED for P120005, P120005/S018, and P120005/S033.

IX.   SUMMARY OF NONCLINICAL STUDIES

The t:slim X2 Insulin Pump software, previously approved under P140015/S020, was modified to include a Predictive Low Glucose Suspend (PLGS) algorithm ("referred to as Basal-IQ" Technology). No new non-clinical laboratory studies were needed for the addition of the Basal-IQ.

The t:slim X2 Insulin Pump with Basal-IQ is the same hardware on the t:slim X2 Insulin Pump (reviewed in P140015/S020). Therefore, no additional testing was conducted. Please see SSED for P140015/S020 for a description of the performance qualification testing (e.g., hardware verification, mechanical hazards test, etc.). For a description of wireless coexistence, electrical safety testing, electromagnetic compatibility testing please see the SSED for P140015/S020. 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. See the SSED for P140015 for the description of biocompatibility testing and for the packaging and sterility process.

Please refer to the SSED for P120005, P120005/S018, and P120005/S033 for pre-clinical testing performed on the Dexcom G5 CGM System.

A. Laboratory Studies

Software Verification and Validation

Software modifications were made to the t:slim X2 Insulin Pump to add the Predictive Low Glucose Suspend (PLGS) algorithm. Comprehensive verification and validation testing was conducted to confirm that the software used in the t:slim X2 Insulin Pump with Basal-IQ 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.

iCGM Use with the t:slim X2 Insulin Pump with Basal-IQ

To support the use of any iCGM sensor (cleared under 21 CFR 862.1355) the sponsor provided a detailed description of the sensor glucose input specifications for the

Basal-IQ algorithm and acceptable clinical and analytical justification demonstrating that he iCGM performance specifications are adequate for safe and effective use of the t:slim X2 Insulin Pump with Basal-IQ system. In addition, the sponsor provided a acceptable plan to assure secure and reliable communication between the t:slim X2 Insulin Pump with Basal-IQ and any iCGM system. As the sponsor follows their communication plan and integrates new iCGM sensors, the labeling for the t:slim X2 Insulin Pump with Basal-IQ will be iupdated to specify any compatible CGMs and iCGMs.

Human Factors Testing

A human factors study was conducted to confirm that the intended users can safely and effectively use the PLGS feature of the t:slim X2 Insulin Pump with Basal-IQ. This involved evaluating usability tasks, such as turning on/off PLGS, setting PLGS alerts, modifying PLGS alerts, and comprehending PLGS alerts. Although the human factors study identified use difficulties with modifying PLGS alerts, these use difficulties did not represent serious use errors since users will still receive the other system alerts (e.g., CGM Low Alert, CGM High Alert, etc.). Therefore, results from the human factors study demonstrates users can safely and effectively use the PLGS feature of the t:slim X2 Insulin Pump.

X.   SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a pivotal study to demonstrate that the Basal-IQ feature of the already approved t:slim X2 Insulin Pump paired with the Dexcom G5 CGM (P400015/S020) can be used safely and that it functions as intended under IDE G170105. The sponsor provided information showing that the Basal-IQ feature of the already approved t:slim X2 pump-CGM device (P140015/S020) functions as intended to stop and resume insulin delivery in response to low and rising glucose levels, respectively. The performance data for the systems generated using the Dexcom G5 was determined to be adequate to represent system performance using iCGM systems.

The sponsor also conducted an analysis of the Basal-IQ algorithm accuracy via simulation using clinical data from Dexcom G5 CGM accuracy study (P120005/S018) that included 50 adult patients and 59 pediatric patients aged 6-17 years old.

A summary of the clinical study and performance data analysis is presented below.

A. Study Design

A total of 107 subjects with Type 1 Diabetes were enrolled at 4 sites in the United States (US). The study was a multi-center, randomized, at home, crossover design evaluation of subjects with type 1 diabetes. Study subjects enrolled were either insulin pump users, multiple daily injection of insulin (MDI) users, CGM naïve users (may be pump or MDI users), or experienced CGM users (may be pump or MDI

users). Of the 107 subjects enrolled (over the age of 6 years old) five subjects did not complete the study (see subject accountability below).

The 102 study subjects participated in a crossover design study, consisting of two 3-week periods with the t:slim X2 Insulin Pump with Basal-IQ (Basal-IQ enabled) used during one period and Sensor Augmented Pump (SAP) used during the other period. The crossover design study was preceded by a run-in phase in which participants received training using the study devices.

Run-in period
The run-in phase consisted of a CGM training period and SAP training period. The CGM training period was 10 to 14 days followed by the SAP training period, which was 14 to 28 days.

Most of the subjects skipped one or both training periods based on the participants' device use at the time of enrollment, as described in the table below.

- Participants currently using a CGM may skip the CGM Training Period per investigator discretion, generally requiring that the CGM has been used on at least 85% of days during the prior 4 weeks.

- Participants currently using a Tandem pump concomitantly with a Dexcom CGM may skip both the CGM Training and the SAP Training periods per investigator discretion.

  o These participants will proceed to the next visit, which can either be the cross over trial randomization visit or the 10-day Basal-IQ pilot period

- Participants must complete the SAP training period if they are either:
  o Not using a CGM
  o Not currently using a Tandem insulin pump

Pilot period
Prior to the initiation of the crossover study, 10 study subjects wore the Dexcom G5 CGM and the t:slim X2 Insulin Pump with Basal-IQ) in a 10-day pilot period. During the pilot period, safety metrics and system usability were evaluated. After 10 days, the participants then transitioned to SAP (t:slim X2 Insulin Pump without the Basal-IQ feature) until all pilot period participants had completed the pilot period. Once this was over, the participants returned to the study center for the crossover trial.

Crossover period
Prior to being randomized into the crossover study, the following procedures were performed:
- Eligibility criteria and individual's desire to participate in the trial was reviewed

- HbA1c measured
- Pregnancy test (performed at both screening and randomizing unless these visits occurred on the same date)
- Study supplies were provided to the participant and randomization assigned

Study subjects who remained eligible to proceed in the crossover trial were randomly assigned to either group A or group B with applicable device training. Participants used the first treatment for three weeks (study period 1) then crossed over to the second treatment for three weeks (study period 2). The two treatment options are the intervention (PLGS) group that will use the t:slim X2 Insulin Pump with Basal-IQ Technology and the control (SAP) group that will use the t:slim X2 Insulin Pump without the Basal-IQ feature. The two groups were:

- Group A: Use of the Dexcom G5 CGM with the t:slim X2 Insulin Pump with Basal-IQ in the first period and use of SAP (t:slim X2 Insulin Pump without Basal-IQ) in the second period
- Group B: Use of the Dexcom G5 CGM with the t:slim X2 Insulin Pump without Basal-IQ (SAP) in the first period and use of the t:slim X2 Insulin Pump with Basal-IQ in the second period

During the two study periods, participants were asked to:
- Use the Study pump and study CGM every day
- Keep the Basal-IQ feature activated if using the Tandem PLGS pump
- Not change pump settings related to insulin delivery (e.g. basal rate) without first discussing with study staff
- Ensure proper calibration of the CGM at all times, using the study-provided glucose meter
- Measure ketones with the study-provided ketone meter when CGM glucose is > 300 mg/dL on awakening or for at least 1 hour at other times, or > 400 mg/dL at any time. CGM glucose > 300 should be confirmed by Self Monitoring Blood Glucose (SMBG) readings
- Contact staff if:
  - Blood ketone readings are ≥ 1.5 mmol/L
  - There are any technical issues with the system
  - There are any symptoms or occurrences of DKA, severe hypoglycemia, or development of other medical problems
  - Pregnancy is possible
  - Discontinuation of study participation is desired

The following parameters were assessed at the end of both study periods:
- Adverse events
- New medical conditions and medications
- HbA1c level
- Basal-IQ usability survey for those completing the use of the t:slim X2 Insulin Pump with Basal-IQ and the Dexcom G5 CGM study period

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the pivotal study was limited to study subjects who met the following inclusion criteria:

   1. Clinical diagnosis, based on investigator assessment, of type 1 diabetes treated with insulin via an insulin pump or injections for at least 1 year, with no major change in the intensity of insulin therapy in the past 3 months (e.g. switching form injections to pump)
   2. Age ≥ 6 years old
   3. For participants <18 years old, living with one or more parents or guardians committed to participating in training and able to contact the participant in case of an emergency
   4. For females, not currently known to be pregnant:
      - If female and sexually active, must agree to use a form of contraception to prevent pregnancy while a participant in the study. A negative serum or urine pregnancy test will be required for all females of child-bearing potential. Subjects who become pregnant will be discontinued from the study. Also, subjects who during the study develop and express the intention to become pregnant within the timespan of the study will be discontinued.
   5. Investigator has confidence that the participant can successfully use all study devices and is capable of adhering to the protocol.

   Study subjects were not permitted to enroll in the pivotal study if they met any of the following exclusion criteria:

   1. Participation in another pharmaceutical or device trial at the time of enrollment or plan to participate in another study during the time period of participation in this study
   2. Employed by, or having immediate family member employed by Tandem; or having a direct supervisor at place of employment who is also directly involved in conducting the clinical trial (as a study investigator, coordinator, etc.); or having a first-degree relative who is directly involved in conducting the clinical trial
   3. A condition, which would put the participant or study at risk including any contraindication to the use of any of the study devices per FDA labelling
      - Individuals should not be enrolled with uncontrolled thyroid disease, renal failure (e.g. dialysis or eGFR < 30), hemophilia or another major bleeding disorder, or unstable cardiovascular disease.
      - Laboratory testing and other work up needed to determine that an individual is a suitable candidate for the study should be performed as part of usual care.
   4. Anticipated need to use acetaminophen during study participation

2. Follow-up Schedule

Basal-IQ Pilot Period
Study subjects were contacted by phone, email, or text on Days 1, 2, and 5 (±1 Day) to assess for adverse events and system issues.

Crossover period
All study subjects were scheduled to return for clinic visits on Days 7 and 21 of each study period to upload the insulin pump data. All patients were contacted on Days 2 and 14 of the study period. At each contact and visit, the occurrence of device issues and adverse events was recorded.

During the final study visit, subjects were asked to complete a survey on the usability of the t:slim X2 Insulin Pump with Basal-IQ and also had blood drawn for a HbA1c test.

3. Clinical Data Analysis

The sponsor assessed the following study metrics:

- Percentage of sensor glucose values < 70 mg/dL.
- Percentage of CGM values <60 mg/dL
- Percentage of values <50 mg/dL
- Area Under the Curve (AUC) CGM glucose <70 mg/dL
- Low blood glucose index[1]
- Frequency of each of the above-listed CGM-measured low glucose metrics
- Mean CGM glucose
- Percentage of CGM values 70 to 180 mg/dL
- Percentage of CGM values >250 mg/dL
- Percentage of CGM values >180 mg/dL
- AUC CGM glucose >180 mg/dL
- High blood glucose index[1]

Safety Analysis:
The following safety outcomes were tabulated for each participant within each 3-week treatment period. The summary statistics included start date, stop date, severity, relationship, resolution, and duration.
- Diabetic ketoacidosis (DKA), as defined by the Diabetes Control and Complications Trial (DCCT).
- Severe clinical hypoglycemic events such that the participant required assistance from another person to actively administer carbohydrate, glucagon, or engage in other resuscitative actions

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1 Kovatchev BP, Cox DJ, Gonder-Frederick LA, Clarke W. Symmetrization of the blood glucose measurement scale and its applications. Diabetes Care 1997;20:1655–1658. Note these metrics are reported by the sponsor; however, the clinical validity with respect to FDA's determination of safe and effective device performance for these specific indices is not clear. We have listed these here as informational.

- Ketosis events (blood ketone level >1.0 mmol/L)
- All other reported adverse events
- Unanticipated adverse device effects

The following outcomes were tabulated separately over 24-hour period, daytime, and nighttime where applicable:
- Insulin delivery including total insulin, basal insulin, and bolus insulin
- Frequency of insulin suspension events and duration of events, including individual suspensions and cumulative suspension time
- CGM glucose nadir during suspension events and peak within 2 hours after events
- The amount of CGM use in both 3-week periods.
- Percentage of time Basal-IQ feature is active.

B. Accountability of PMA Cohort

A total of 107 subjects entered the run-in phase of which 4 subjects withdrew prior to randomization. One subject did not wish to continue in the study and withdrew and one subject did not wish to continue wearing the sensor. One subject experienced multiple occlusion and incomplete bolus alerts within 24 hours of the run-in phase and on multiple occasions during the week, which resulted in high glucose levels and discomfort. One subject had multiple site failures in the first 24 hours wearing the pump during the run-in phase, and the subject's parent had job commitments and could not comply with study follow-up visits.

Of the remaining 103 subjects, 52 were randomized to Group A (use of Basal-IQ first followed by SAP use) while 51 were randomized to Group B (use of SAP first followed by Basal-IQ use).

One subject (Group B) reported multiple device issues (Bluetooth connectivity and reservoir filling) while participating in the first of the two crossover periods. Due to this and to lengthy travel distance to and from the site, the subject decided to withdraw participation and did not complete the follow-up visit requirements. Therefore, 102 subjects completed the crossover study.

C. Study Population Demographics and Baseline Parameters

See Tables 1 and 2 for a description of the demographics and baseline characteristics of the study population subjects entering the crossover phase of the study.

Table 1: Demographics Information

Demographic	Overall (N=103)	Basal-IQ First (N=52)	SAP First (N=51)
Age (years) Mean ± SD	24 ± 17	25 ± 18	23 ± 16

Demographic	Overall (N=103)	Basal-IQ First (N=52)	SAP First (N=51)
Median (quartiles)	16 (13, 31)	17 (12, 34)	16 (13, 25)
Range	6 to 72	7 to 64	6 to 72
< 18 years old (%)	60 (58%)	29 (56%)	31 (61%)
≥ 18 years old (%)	43 (42%)	23 (4%)	20 (39%)
Sex			
Male, N (%)	45 (44%)	26 (50%)	19 (37%)
Female, N (%)	53 (56%)	26 (50%)	32 (63%)
Race			
White non Hispanic, N (%)	82 (80%)	44 (85%)	38 (75%)
Black non Hispanic, N (%)	2 (2%)	0 (0%)	2 (4%)
Hispanic or Latino, N (%)	7 (7%)	3 (6%)	4 (8%)
Asian, N (%)	3 (3%)	2 (4%)	1 (2%)
Native Hawaiian/Other Pacific Islander, N (%)	1 (< 1%)	1 (2%)	0 (0%)
More than one race, N (%)	8 (8%)	2 (4%)	6 (12%)

Table 2: Baseline Characteristics

Demographic	Overall (N=103)	Basal-IQ First (N=52)	SAP First (N=51)
Diabetes Duration (years)			
Median (quartiles)	8 (3, 16)	9 (3, 19)	7 (3, 13)
Range	1 to 52	1 to 52	1 to 51
Body mass index (kg/cm2)			
Mean ± SD	23 ± 5	23 ± 4	23 ± 5
HbA1c (%)			
Mean ± SD	7.3 ± 0.9	7.2 ± 0.9	7.4 ± 0.9
Current Insulin Modality			
Injections	17 (17%)	9 (17%)	8 (16%)
Pump	86 (83%)	43 (83%)	43 (64%)
Past amount of pump use			
3 months to < 6 months	2 (2%)	0 (0%)	2 (5%)
6 months to < 1 year	2 (2%)	1 (2%)	1 (2%)
1 year to < 2 years	10 (12%)	4 (9%)	6 (14%)
2 years to < 5 years	22 (26%)	12 (28%)	10 (23%)
≥ 5 years	50 (58%)	26 (60%)	24 (56%)
CGM use status			
Current	87 (84%)	45 (87%)	42 (82%)
In past, but not current	14 (14%)	6 (12%)	8 (16%)
Never	2 (2%)	1 (2%)	1 (2%)
Days of CGM use in past			
< 3 months	1 (<1%)	0 (0%)	1 (2%)
3 months to < 6 months	2 (2%)	0 (0%)	2 (4%)
6 months to < 1 year	1 (<1%)	1 (2%)	0 (0%)

Demographic	Overall (N=103)	Basal-IQ First (N=52)	SAP First (N=51)
1 year to < 2 years	5 (5%)	3 (6%)	2 (4%)
2 years to < 5 years	4 (4%)	3 (6%)	4 (8%)
5 to < 10 years	14 (14%)	10 (19%)	4 (8%)
≥ 10 years	76 (74%)	35 (67%)	41 (80%)

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on 102 subjects. The key safety outcomes for this study are presented below. There were no unanticipated adverse device effects or serious adverse events reported. The number of ketosis events (calendar day with blood ketone level > 1.0 mmol/L) between the two treatment options (Basal-IQ enabled vs SAP) was comparable with 99 days of ketosis events for the Basal-IQ enabled arm and 95 days of ketosis events for the SAP arm.

Adverse effects that occurred in the PMA clinical study:

There was a total of two serious adverse events that occurred during the course of the study. The two serious adverse events were reported by two subjects in the SAP cohort of Group B (Use of SAP in the first period and use of the study device in the second period).

- One subject experienced a bowel obstruction that required temporary removal of the study device while hospitalized.
- Another subject experienced a severe hypoglycemic event where the system alarmed appropriately. The subject initially attempted self-treatment with oral carbohydrates, but the blood glucose value was still below 70 mg/dL. The subject eventually required assistance of another person to actively administer glucagon. The subject had complete recovery on the same date.

Both events were unrelated to the Basal-IQ technology and unrelated to the study procedure.

Other analyses:

The following metrics were tabulated separately over 24-hour period, daytime, and nighttime where applicable:
- Insulin delivery including total insulin, basal insulin, and bolus insulin
- Frequency of insulin suspension events and duration of events, including individual suspensions and cumulative suspension time
- CGM glucose nadir during suspension events and peak within 2 hours after events
- The amount of CGM use in both 3-week periods.
- Percentage of time PLGS is active.

These metrics were comparable between the two arms (Basal-IQ enabled vs SAP).

Table 3: Insulin Delivery Differences

Characteristic	Unit of Measure Average ± Standard Deviation	Basal-IQ	SAP
Total Insulin Units	24-hour period	44.6 ± 20	45.9 ± 20.2
	Daytime (6 AM to 10 PM)	35.6 ± 15.6	36.5 ± 15.4
	Nighttime (10 PM to 6 AM)	9.0 ± 5.3	9.4 ± 5.6
Basal Insulin Units	24-hour period	20.3 ± 10.4	21.5 ± 10.5
	Daytime (6 AM to 10 PM)	14.1 ± 7.4	15.0 ± 7.4
	Nighttime (10 PM to 6 AM)	6.2 ± 3.2	6.5 ± 3.2
Bolus Insulin Units	24-hour period	24.5 ± 12.4	24.5 ± 12.5
	Daytime (6 AM to 10 PM)	21.6 ± 10.8	21.6 ± 10.4
	Nighttime (10 PM to 6 AM)	2.9 ± 2.9	2.9 ± 3.4

Table 4: Frequency of Insulin Suspension Events per Subject-Day (N=102)

Frequency of Insulin Suspension Events per Subject-Day	24-hour	Day (6AM to 10 PM)	Night (10 PM to 6 AM)
Percentile			
Min	0	0	0
10th	1	0	0
25th	2	2	0
50th	5	3	1
75th	8	6	3
90th	12	8	5
Max	24	24	12

Table 5: Duration of Insulin Suspensions (minutes) (N=102)

	Minutes per Individual Suspension		
	24-hour	Day (6AM to 10 PM)	Night (10 PM to 6 AM)
Percentile			
Min	5	5	5
10th	5	5	5
25th	5	5	5
50th	10	10	10
75th	25	25	20
90th	40	40	40
Max	120	120	120

Table 6: Cumulative Suspension Time per Subject-Day (N=102)

Cumulative Suspension Time Per Subject-Day (min)	24-hour	Day (6AM to 10 PM)	Night (10 PM to 6 AM)
Percentile			
Min	0	0	0
10th	5	0	0
25th	40	20	0
50th	90	60	10
75th	155	110	55
90th	215	160	95
Max	530	350	255

Table 7: CGM Glucose Nadir During Suspension Events (mg/dL) (N=102)

	24-hour	Day (6AM to 10 PM)	Night (10 PM to 6 AM)
Percentile			
Min	40	40	40
10th	57	57	56
25th	69	69	68
50th	82	82	81
75th	96	97	94
90th	115	117	111
Max	263	225	263

Table 8: CGM Use Over 21-Day Period by Study Arm (N=102)

Percentage of Time Using CGM	Basal-IQ	SAP
Median (quartiles) [min to max]	95% (90%, 97%) [20% to 98%]	94% (89%, 96%) [27% to 98%]
≥ 90%	76 (75%)	74 (73%)
80% to < 90%	21 (21%)	20 (20%)
70% to < 80%	3 (3%)	3 (3%)
60% to < 70%	0 (0%)	2 (2%)
50% to < 60%	1 (<1%)	1 (< 1%)
< 50%	2 (2%)	2 (2%)

Table 9: Amount of Basal-IQ Technology Use over the 21-Day Period (N=102)[*]

Percent time using the Basal-IQ Feature	Number of Subjects	Percent of Study Population

≥ 90%	90	88%
80% to < 90%	9	9%
70% to < 80%	1	< 1%
60% to < 70%	1	< 1%
50% to < 60%	0	0%
< 50%	1	< 1%

*Denominator is the total possible time within 21-day post-randomization study period. Basal-IQ Technology use includes time in which Basal-IQ Technology was on and available, on and suspended, and on and unavailable. The Basal-IQ Technology could be on and unavailable due to unavailable real-time CGM data or various pump statuses (e.g., total suspend time exceeds 120 minutes within a 150-minute period, user-override is active [manual resume], a standard bolus is in progress, no sensor session active, pumping is not started, EGV is above 229 mg/dL, or too many missed readings).

2. Effectiveness Results

The performance data shown below demonstrate that the Basal-IQ feature of the approved t:slim X2 Insulin Pump paired with the Dexcom G5 CGM (P140015/S020) functions as intended to stop and resume insulin delivery in response to low and high glucose levels, respectively.

This clinical study was not designed to collect information on clinical effectiveness endpoints. The following is information regarding the observed performance of the system between the two study arms.

The table below provides information on the percentage of sensor glucose values < 70 mg/dL, for all subjects who completed the study (N=102). This parameter was calculated for each study subject in each of the 3-week treatment periods by pooling all sensor glucose readings that occurred within each 21-day period. All sensor glucose readings were weighted equally in the pooled percentages regardless of how they distributed across the 21 days. The percentage in the Basal-IQ timeframe was then compared to the percentage in the SAP arm for the same participant.

Table 2 Percent of CGM Glucose Sensor Values < 70 mg/dL (N=102)

Hours of Data	Basal-IQ enabled	SAP
Hours of CGM data available for analysis (Quartiles) [Min-Max]	473 (447, 485) [98-495]	467 (447, 482) [132-494]
Percent of CGM glucose sensor values < 70 mg/dL		
Median (quartiles)	2.6% (1.4%, 4.0%)	3.2% (1.9%, 6.1%)
Mean ± SD	3.1% ± 2.8%	4.5% ± 3.9%
< 1%	21 (21%)	12 (12%)

1% to < 2%	19 (19%)	15 (15%)
2% to < 3%	18 (18%)	20 (20%)
3% to < 5%	30 (29%)	23 (23%)
≥ 5%	14 (14%)	32 (31%)

The table below compares the time spent in low sensor glucose value ranges, time spent in high sensor glucose value ranges, the mean sensor glucose value, and percentage of sensor values 70 to 180 mg/dL at baseline and for each arm of the study. The average glucose in the Study Arm during Daytime was 160 ± 26 mg/dL and 157 ± 29 mg/dL during Nighttime. In the SAP arm the average glucose during Daytime was 160 ± 27 mg/dL and 159 ± 30 md/dL during Nighttime. The results in the Basal-IQ group were similar to the SAP (Control) group. The information in the table below is not meant to support a determination of clinical effectiveness.

Characteristic	Baseline	Basal-IQ Enabled	SAP
Hours of Data Median (quartiles)	312 (297, 560)	473 (447, 485)	467 (447, 482)
Mean sensor glucose (mg/dL) ± SD	158 ± 27	159 ± 25	159 ± 27
Percent of sensor glucose 70-180 mg/dL ± SD	64% ± 15%	65% ± 15%	63% ± 15%
Median Sensor Glucose < 60 mg/dL (quartiles)	1.2% (0.6%, 2.1%)	0.9% (0.4%, 1.6%)	1.2% (06%, 2.7%)
Median Sensor Glucose < 50 mg/dL (quartiles)	0.3% (0.1%, 0.6%)	0.2% (0.1%, 0.5%)	0.3% (0.1%, 0.7%)
Median Area over curve Sensor glucose < 70 mg/dL (quartiles)	0.3 (0.2, 0.5)	0.2 (0.1, 0.4)	0.3 (0.2, 0.7)
Median Low blood glucose index[2] (quartiles)	0.9 (0.6, 1.3)	0.8 (0.5, 1.1)	0.9 (0.6, 1.5)
Median hypo events per week[*] (quartiles)	1.1 (0.5, 2.4)	0.8 (0.3, 1.9)	1.1 (0.4, 3.0)
Median Sensor Glucose > 250 mg/dL (quartiles)	7% (3%, 15%)	8% (3%, 13%)	8% (3%, 16%)
Median Sensor Glucose > 180 mg/dL (quartiles)	32% ± 17%	32% ± 15%	33% ± 16%
Median Area over curve sensor glucose > 180 mg/dL (quartiles)	15 (7, 25)	16 (8, 24)	17 (7, 26)

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2 Kovatchev BP, Cox DJ, Gonder-Frederick LA, Clarke W. Symmetrization of the blood glucose measurement scale and its applications. Diabetes Care 1997;20:1655–1658. Note these metrics are reported by the sponsor; however, the clinical validity with respect to FDA's determination of safe and effective device performance for these specific indices is not clear. We have listed these here as informational.

Median High blood glucose index[2] (quartiles)	7 (4, 10)	7 (4, 10)	7 (4, 10)

*A "hypo event" was defined as at least 2 sensor values < 54 mg/dl that are 15 or more minutes apart with no intervening values > 54 mg/dl. At least 2 sensor values > 70 mg/dl that are 30 or more minutes apart with no intervening values < 70 mg/dl, were required to end a "hypo event."

Basal-IQ Performance
The Basal-IQ (PLGS algorithm) performance was evaluated by reanalyzing the clinical data from Dexcom G5 CGM clinical accuracy studies (P120005) through the Basal-IQ algorithm to obtain 'true suspend,' 'false suspend' and 'missed suspend' rates, and 'true resume,' 'false resume' and 'missed resume' rates. For the Dexcom G5 CGM study, reference glucose values obtained from a laboratory blood glucose comparator method (CM) were collected every 15 minutes and compared to corresponding CGM values in 50 adult patients and 59 pediatric patients aged 6-17 years old. The Basal-IQ algorithm was retrospectively applied to each subject's CGM trace from the Dexcom G5 CGM study and the corresponding CM values were used as a comparator to determine whether the Basal-IQ algorithm appropriately suspended or resumed insulin. Each 5-minute insulin suspension and resumption action was then determined to be in 1 of 3 categories; True, False or Missed. Specifically, the evaluation rules are these:

The Basal-IQ algorithm suspends insulin in either of these two conditions:
- Current CGM value is < 70 mg/dl, or
- 30-minute predicted CGM value is < 80 mg/dl

And resumes insulin delivery in either of these two conditions:
- Current CGM value is increasing, or
- Both of the above two suspension rules are no longer true

Suspension Rules:

TRUE suspend	Basal-IQ commanded suspend and blood glucose < 80 occurred within 30 minutes
FALSE suspend	Basal-IQ commanded suspend and no blood glucose < 80 occurred within 30 minutes
MISSED suspend	(blood glucose < 80) and (blood glucose < previous blood glucose) with no Basal-IQ commanded suspend in preceding 30 minutes

Resume Rules:

TRUE Resume	Basal-IQ commands resume and blood glucose > previous blood glucose or (current blood glucose ≥ 70 and in 30-minutes blood glucose > 80)
FALSE Resume	Basal-IQ commands resume and blood glucose ≤ previous blood glucose and (current blood glucose < 70 or in 30-minutes blood glucose > 80)

MISSED Resume	Basal-IQ remains suspended and current blood glucose has increased by ≥ 1

The results from the analysis from 109 subjects (aged 6-86 years old) are as follows:

*Suspend Summary	Total	Percent
TRUE Resumes	1518	83.91%
FALSE Resumes	240	13.27%
MISSED Resumes	51	2.82%
Total Events	1809	100.00%

*Predictive and Threshold

The Resume Actions were analyzed at the first opportunity to resume insulin based on the CM data, then 5 minutes later and 10 minutes later.

Resume Summary	Resume Actions (%)		
	0 minutes	+ 5 minutes	+ 10 minutes
TRUE Resumes	219 (46.4%)	219 (60.5%)	219 (68.9%)
FALSE Resumes	62 (13.1%)	62 (17.1%)	62 (19.5%)
MISSED Resumes	191 (40.5%)	81 (22.4%)	37 (11.6%)
Total Events	472 (100%)	362 (100%)	318 (100%)

3. Subgroup Analyses

Data for the t:slim X2 Insulin Pump with Basal-IQ and without Basal-IQ was evaluated within study population subgroups, such as age (< 18 years old, ≥ 18 years old), duration of type 1 diabetes (< 8 years and ≥ 8 years), baseline HbA1c (< 8.0% and ≥ 8.0%), and baseline time of glucose sensor values below 70 mg/dL (< 5% and ≥ 5%).

Although the studies were not powered for analysis of subpopulations, no significant differences in performance were noted based on these subgroup analyses.

4. Pediatric Extrapolation

This device is intended for use in people ≥ 6 years old. In this premarket application, existing clinical data was not leveraged to support approval of in pediatric patients less than 6 years of age.

E. Financial Disclosure

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

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

In accordance with the provisions of section 515(c)(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 performance data presented above demonstrates that the Basal-IQ feature of the already approved t:slim X2 Insulin Pump paired with the Dexcom G5 CGM (P140015/S020) can be used safely and that it functions as intended. The sponsor's analysis of input specifications is adequate to assure reasonable safety and effectiveness when iCGM sensors are used with the system as well. Additionally, the performance data demonstrates that the Basal-IQ feature functions as intended to stop and resume insulin delivery in response to low and high glucose levels, respectively.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory data (described above), on the data collected in a clinical study conducted to support PMA approval of the Dexcom G5 Platinum CGM System as described in the SSED for P120005/S033, and on the clinical study (described above).

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.

Potential CGM-related complications:

- Sensor breakage with fragments under the skin is a potential, but uncommon adverse event related to the CGM. 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 with Basal-IQ 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.

A potential adverse effect associated with the Basal-IQ feature of the insulin pump is hyperglycemia due to inappropriate suspension of insulin delivery.

There were two adverse events reported for two subjects in the SAP arm (Group B) using the t:slim X2 Insulin Pump without Basal-IQ. Both events (severe hypoglycemia and bowel obstruction) were adjudicated as not related to the study treatment, study procedure, or the investigational device. No serious adverse effects or unanticipated adverse device effects (UADE) were reported in the clinical study.

The long term risks of use of the device is unclear due to the insufficient patient numbers and insufficient follow up to detect uncommon but serious events (e.g. DKA, severe hypoglycemia); however, there has been no post-market signal to indicate sensor augmented insulin pump therapy is associated with increased risk compared to other standard of care diabetes treatment modalities.

C. **Benefit-Risk Determination**

Benefits

The probable benefits of the device (t:slim X2 Insulin Pump with Basal-IQ paired with Dexcom G5 CGM or iCGM) are based on data collected in clinical and nonclinical studies conducted to support PMA approval as described above and in P140015/S020 and P120005/S033.

The addition of the Basal-IQ feature of the t:slim X2 insulin pump is beneficial to patients since it includes the ability for users to set the system to automatically suspend delivery of insulin when the predicted glucose value falls below 80 mg/dL. After insulin is suspended, delivery resumes when the system detects glucose values begin to rise. The Basal-IQ feature is an added mitigation to detect and mitigate hypoglycemia and hyperglycemia excursion. The safety of the device with the Basal-IQ feature (described in Section X.d. Safety and Effectiveness Results, above) appears to be at least comparable to the performance of the device without the Basal-IQ feature.

The benefits of the t:slim X2 Insulin Pump with Basal-IQ paired with Dexcom G5 CGM otherwise remain unchanged from P140015/S020. These benefits include display of CGM glucose values every 5 minutes, trend arrows, and rate of change glucose alerts. Thus, the t:slim X2 with Basal-IQ can assit in detection and prevention of hypoglycemia and hyperglycemia glucose excursions. The device can also provide a more comprehensive understanding of glucose trends and patterns in response to activities of daily living as well as during times of illness, erratic eating, and variable physical activity.

The t:slim X2 Insulin Pump with Basal-IQ can be used with a compatible iCGM. There is currently only one iCGM (i.e., Dexcom G6 iCGM) currently authorized for marketing in the US; however, other iCGMs that are FDA cleared in the future and become available may be integrated into the t:slim X2 with Basal-IQ and provide patients and healthcare providers the option to better optimize sensor functionality with individual patient needs without compromising the performance of the t:slim X2 Insulin Pump with Basal-IQ.

Risks

The addition of the Basal-IQ feature is not expected to pose additional risks that translate to harm to patients, given that the performance of the device with Basal-IQ is at least comparable to the device without Basal-IQ. Although there were no DKA events or an increase in ketosis events during the clinical study, there is a potential for these events given the suspension of insulin inherent in the Basal-IQ feature. Additional potential risks include hypoglycemia from over-delivery of insulin due to

pump defect or hyperglycemia due to pump or insulin set failure, and are further assessed under P140015/S020.

Overall, the ability of the Basal-IQ feature to accurately suspend and resume appear clinically acceptable. The duration of false or missed resumptions and suspensions are not expected to occur for extended periods of time since the device reassesses whether to resume or suspend every 5 minutes. Therefore, there do not appear to be additional questions of safety or effectiveness that arise as a result of this performance.

The risks of the sensor-enabled pump functionality of the t:slim X2 Insulin Pump with Basal-IQ otherwise remain unchanged from those assessed under P140015/S020.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

FDA considered that patients want a variety of devices that provide information and aid in management of their glucose control to inform decision making with their health care providers on lifestyle changes and treatment decisions. Patients have also expressed at patient centered forums, on social media outlets, and in personal conversations with FDA staff that they want devices that provide features that enable automated insulin suspension, and are willing to accept reasonable risks related to such devices. This information was gathered during patient oriented conferences and face-to-face meetings with patients.

Conclusion

In conclusion, given the available information above, the data support that for the indications for use of the t:slim X2 Insulin Pump with Basal-IQ the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application (as well as data referenced from previously approved premarket applications) 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 Insulin Pump with Basal-IQ outweigh the risks.

XIII. CDRH DECISION

CDRH issued an approval order on June 21, 2018.

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. <u>APPROVAL SPECIFICATIONS</u>

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. <u>REFERENCES</u>

None.