EVALUATION OF AUTOMATIC CLASS III DESIGNATION FOR
t:slim X2 insulin pump with interoperable technology
DECISION SUMMARY

A. DEN Number:

DEN180058

B. Purpose for Submission:

De Novo request for evaluation of automatic class III designation for the t:slim X2 insulin pump with interoperable technology

C. Manufacturer and Device Name:

Tandem Diabetes Care, Inc. and the t:slim X2 insulin pump with interoperable technology

D. Type of Test or Tests Performed:

Not applicable.

E. System Descriptions:

1. Device Description:
   The t:slim X2 insulin pump with interoperable technology (as shown in Figure 1) 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. The device includes a custom disposable cartridge which is motor-driven to deliver patient programmed basal rates and boluses through an infusion set into subcutaneous tissue.

   The t:slim X2 insulin pump with interoperable technology consists of:
   - a user-operated interface display;
   - an electronic microprocessor software control system, including Bluetooth radio module and signal processing algorithms allowing the pump to communicate with digitally connected devices;
   - motor and encoder;
   - rack drive mechanism; and
   - an audible speaker and a vibrator to provide alarms, alerts and reminders to the user.

Figure 1: The t:slim X2 insulin pump with interoperable technology

The front of the t:slim X2 insulin pump with interoperable technology includes a color touch screen display that has a capacitive touch panel that detects a finger touch. The Screen On Button on the side of the pump is surrounded by an LED indicator light. This button is used to turn on the touch screen display so that the user can operate their pump. The Screen On Button also provides users with a quick bolus option, which is a feature that allows a user to program and deliver a bolus of insulin through a sequence of presses, without use of the touch screen. The pump provides audio and vibratory feedback to the user to confirm delivery.

An electrically-isolated USB port is located on one end of the pump, which is covered by a protective rubber door. The USB port is accessible to patients and when connected with a power supply is used to charge the internal lithium polymer battery or download data to and from a computer. The pump provides the user with an indication of the remaining battery power on the display and alerts when the battery power is low.

The pump features three separate microprocessors; two controlling the pump functionality, and a third for controlling the Bluetooth Low Energy (BLE) radio. The pump is capable of sending and receiving data to and from other interoperable devices. The pump is designed to act on commands from other authorized digital pump controller devices to adjust insulin dosing. The pump is designed to be able to receive and display alerts and alarms to users based on information received from other interoperable devices.

The insulin cartridge is designed to hold up to 3 mL, or 300 units, of U-100 insulin. It is for single use and is intended to be replaced at least once every three days, depending on an individual's specific insulin usage or the indications for use of the insulin. The insulin fill port is a septum on the cartridge head, through which the patient fills the insulin

reservoir. The patient line is an access point for connecting an infusion set for insulin delivery.

In addition to the above described primary components of the device, the device is intended to be used with:

- FDA cleared insulin infusion sets with a tubing connector supplied separately;
- 3.0 mL syringe and fill needle.
- Wall charger, power supplies with USB for charging the pump's internal battery;
- Belt clip; and
- Digitally connected devices identified in the device labeling.

2. Principles of Operation:

To operate the pump, a patient must first be trained on its setup and use, based on the instructions within the User's Guide. The desired timing and quantity of insulin delivery (bolus or basal) is programmed by the patient based on their healthcare provider's recommendations. The patient uses the Screen On/Quick Bolus button and touch screen to control and monitor insulin delivery.

The software included in the t:slim X2 insulin pump with interoperable technology also controls the following features:

- Basal Therapy – directing delivery of a continuous flow rate of insulin;
- Bolus Therapy – directing delivery of bolus of insulin;
- Safety Monitoring – occlusion detection and notification of low battery or insulin reservoir;
- Self Testing, Error Tracking, and Diagnostics
- Data logging – including delivery history, commands and confirmations, connectivity states, malfunctions, alarms;
- Information security, including confidentiality, integrity, availability, and accountability (CIAA)
- Secured Wireless communication, including event logging and digital interfacing with interoperable devices
- Failsafe design features in case of interruption of communication with digitally connected devices;

3. Modes of Operation:

Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

Yes ___X___ or No _____

Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

Yes __X____ or No _____

4. Specimen Identification:

   Not applicable.

5. Specimen Sampling and Handling:

   Not applicable.

6. Calibration:

   Calibration of motor gearbox backlash values to ensure motor movement correlates with commanded fluid delivery volume is applied during manufacturing.

7. Quality Control:

   Not applicable.

8. Software:

   FDA has reviewed applicant's Hazard Analysis and Software Development processes for this line of product types:

   Yes___X____ or No_____

F. Regulatory Information:

1. Regulation section: 21 CFR 880.5730
2. Classification: Class II
3 Product code: QFG
4. Panel: 75, Clinical Chemistry

G. Indications For Use:

1. Indication(s) for Use:

   The t:slim X2 insulin pump with interoperable technology (the 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 Pump is able to reliably and securely communicate with compatible, digitally connected devices, including automated insulin dosing software, to receive, execute, and confirm commands from these devices. The Pump is intended for single patient, home use and requires a prescription. The Pump is

indicated for use with NovoLog/NovoRapid or Humalog U-100 insulin. The Pump is indicated for use in individuals 6 years of age and greater.

2. Special Conditions for Use Statement(s):

This device is for prescription use only.

Remove this device before Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, or high-frequency electrical heat (diathermy) treatment. The magnetic fields and heat could damage the components of the t:slim X2 insulin pump with interoperable technology.

H. Standards Documents/Guidance Documents Referenced (if applicable):

ISO 14971:2007: Medical Devices - Application of Risk Management to Medical Devices FDA Recognition No: 5-40

ANSI/AAMI/IEC 62366-1:2015 Medical Devices – Application of usability engineering to medical devices

ANSI/AAMI HE75:2009 Human factors engineering, Design of medical devices

60601-1-2: Edition 3:2007-03 Medical Electrical Equipment - part 1-2: General requirements for basic safety and essential performance - Collateral Standard: electromagnetic compatibility - requirements and tests. (General I (QS/RM)) FDA Recognition No: 19-2

ES60601- 1:2005/(R)2012 and A1:2012,, c1:2009/(r)2012 and a2:2010/(r)2012 Medical Electrical Equipment - part 1: General requirements for basic safety and essential performance (IEC 60601- 1:2005, mod). General I (QS/RM)) FDA Recognition No: 19-4, 19-5

ASTM D4169: Standard Practice for Performance Testing of Shipping Containers and Systems

I. Performance Characteristics*:*

The t:slim X2 insulin pump with interoperable technology is similar to the t:Slim insulin pump (P140015) and the t:Slim X2 insulin pump P180008. The hardware and much of the software are identical. The t:slim X2 insulin pump with interoperable technology has some modified software. The sponsor referenced P140015 and P190008 for many analytical studies and software documentation.

1. Analytical Performance:

   a. Basal delivery accuracy

      To assess basal delivery accuracy, thirty two pumps were tested by delivering water

at low, medium, and high basal rates (0.1, 2.0, and 15 U/hr). Sixteen of the pumps were new, and sixteen had been aged to simulate 4 years of typical regular use. For both aged and unaged pumps, eight each were tested with a new cartridge, and eight with a cartridge which had undergone 2 years of real time aging. The water was pumped into a container on a scale, and the weight of the water at various times points was used to assess basal delivery accuracy.

The following tables report the basal delivery performance as the total amount of fluid delivered over a specific time period. The basal delivery accuracy performance of new and aged pumps and new and aged cartridges was similar. Results are reported as the median total amount of fluid delivered for all pumps tested, and the lowest and highest delivery amounts observed for any individual pump tested at low, medium, and high basal rates. For the intermediate and high rates, delivery was measured starting from the time that delivery was first commanded, with no warm-up period. For the minimum basal rate, delivery was analyzed following a 1-hour delivery warm-up period. Tables 1-3 below show the duration of fluid delivery in the first row, the amount of fluid that should have been delivered in the second row, and the median, minimum, and maximum amount that was actually delivered by the pumps tested in the third row.

Table 1: Amount of fluid delivered after 1, 6, and 12 hours with 15 U/hr (high) basal rate setting

15 U/hr Basal Duration	**1 hour**	**6 hours**	**12 hours**
Total expected delivery volume	**15 U**	**90 U**	**180 U**
Median amount delivered [min, max]	15.4 U [14.7, 15.7]	90.4 U [86.6, 93.0]	181 U [175, 187]

Table 2: Amount of fluid delivered after 1, 6, and 12 hours with 2 U/hr (medium) basal rate setting

2 U/hr Basal Duration	**1 hour**	**6 hours**	**12 hours**
Total expected delivery volume	**2 U**	**12 U**	**24 U**
Median amount delivered [min, max]	2.1 U [2.1, 2.2]	12.4 U [12.0, 12.8]	24.3 U [22.0, 24.9]

Table 3: Amount of fluid delivered after 1, 6, and 12 hours with 0.1 U/hr (low) basal rate setting

0.1 U/hr Basal Duration	**1 hour**	**6 hours**	**12 hours**
Total expected delivery volume	**0.1 U**	**0.6 U**	**1.2 U**
Median amount delivered [min, max]	0.12 U [0.09, 0.16]	0.67 U [0.56, 0.76]	1.24 U [1.04, 1.48]

b. Bolus delivery accuracy

To assess bolus delivery accuracy, thirty two pumps were tested by delivering consecutive low, medium, and high bolus volumes (0.05, 2.5, and 25 units). Sixteen of the pumps were new, and sixteen had been aged to simulate 4 years of regular use. For both aged and unaged pumps, 8 each were tested with a new cartridge, and 8 with a cartridge which had undergone 2 years of real time aging. The number of total and consecutive boluses delivered in this testing for each delivery volume is described in Table 4 below:

Table 4: Summary of bolus testing protocol

Bolus size (units)	Number of pumps tested	Consecutive boluses per pump	Total boluses
0.05 units	32	25	800
2.5 units	32	25	800
25 units	32	8	256

Water was used as a substitute for insulin for this testing. The water was pumped into a container on a scale, and the weight of the liquid at various times points was used to assess bolus delivery accuracy.

The actual bolus volume delivered was compared to the expected bolus volume for minimum, intermediate, and maximum boluses. Tables 5-7 below show the number (and %) of boluses within the specified range of each target bolus volume. For example, for the 2.5 unit bolus test, 753 of the 800 total test boluses (94.1%) were between 2.375 and 2.625 units (i.e., they were between 95% and 105% of the expected delivered bolus volume), while 14 of the 800 total test boluses (1.8%) were between 0.625 and 1.875 units (i.e., they were between 25% and 75% of the expected delivered bolus volume).

Table 5: Amount of fluid delivered after a 0.05U bolus request

Units delivered after a 0.05U bolus request (% of commanded units)										
	<0.0125 (<25%)	0.0125 - 0.0375 (25-75%)	0.0375-0.045 (75-90%)	0.045-0.0475 (90-95%)	0.0475-0.0525 (95-105%)	0.0525-0.055 (105-110%)	0.055-0.0625 (110-125%)	0.0625-0.0875 (125-175%)	0.0875-0.125 (175-250%)	>0.125 (>250%)
Number and percent of boluses	21/800 (2.6%)	79/800 (9.9%)	63/800 (7.9%)	34/800 (4.25%)	272/800 (34.0%)	180/800 (22.5%)	105/800 (13.1%)	29/800 (3.6%)	17/800 (2.1%)	0/800 (0.0%)

Table 6: Amount of fluid delivered after a 2.5U bolus request

Units delivered after a 2.5U bolus request (% of commanded units)										
	<0.625 (<25%)	0.625-1.875 (25-75%)	1.875-2.25 (75-90%)	2.25-2.375 (90-95%)	2.375-2.625 (95-105%)	2.625-2.75 (105-110%)	2.75-3.125 (110-125%)	3.125-4.375 (<125-175%)	4.375-6.25 (175-250%)	>6.25 (>250%)
Number and percent of boluses	9/800 (1.1%)	14/800 (1.8%)	11/800 (1.4%)	8/800 (1.0%)	753/800 (94.1%)	5/800 (0.6%)	0/800 (0.0%)	0/800 (0.0%)	0/800 (0.0%)	0/800 (0.0%)

Table 7: Amount of fluid delivered after a 25U bolus request

Units delivered after a 25U bolus request (% of commanded units)										
	<6.25 (<25%)	6.25-18.75 (25-75%)	18.75-22.5 (75-90%)	22.5-23.75 (90-95%)	23.75-26.25 (95-105%)	26.25-27.5 (105-110%)	27.5-31.25 (110-125%)	31.25-43.75 (125-175%)	43.75-62.5 (175-250%)	>62.5 (>250%)
Number and percent of boluses	0/256 (0.0%)	0/256 (0.0%)	1/256 (0.4%)	3/256 (1.2%)	252/256 (98.4%)	0/256 (0.0%)	0/256 (0.0%)	0/256 (0.0%)	0/256 (0.0%)	0/256 (0.0%)

The bolus accuracy performance of new and aged pumps and new and aged cartridges was similar. However, differences in performance were observed between individual pump test setups.

For example, when delivering 25 repeated small boluses (0.05 U):

- The best performing pump test setup delivered 18 out of 25 of those boluses within +/- 5% of the requested 0.05 U dose, 21 out 25 boluses within +/- 10% of the requested 0.05 U dose, and 24 out of 25 boluses within +/- 15% of the requested 0.05 U dose.

- The worst performing pump test setup delivered 2 out of 25 boluses within +/- 5%% of the requested 0.05 U dose, 9 out of 25 boluses within +/- 10%% of the requested 0.05 U dose, and 11 out of 25 boluses within +/- 15% of the requested 0.05 U dose.

  At the intermediate bolus size of 2.5 units these same pumps performed in the following way:

- The best performing pump test setup delivered 25 out of 25 of those boluses within +/- 5% of the requested 2.5 U dose.

- The worst performing pump test setup delivered 21 out of 25 boluses within +/- 5% of the requested 2.5 U dose, 21 out of 25 boluses within +/- 10% of the requested 2.5 U dose, and 22 out of 25 boluses within +/- 15% of the requested 2.5 U dose.

c. Occlusion detection:

To assess the ability of the pump to detect occlusions in the device fluid path, 29 pumps were assessed by delivering water while connected to a representative 110 cm infusion set. To evaluate bolus occlusion detection, each pump was commanded to deliver boluses of 3 units and 25 units, and the distal end of the infusion set was occluded. To evaluate basal occlusion detection, each pump was commanded to deliver a basal rate of 2.0 units per hour, and the distal end of the infusion set was occluded. For each test, the time between occlusion and pump detection of occlusion was determined. The average time and maximum time between occlusion and occlusion detection for each test condition is described in Table 8 below:

Table 8: Time to Occlusion Detection for Bolus and Basal Delivery

	Average time to occlusion detection (h:mm:ss)	**Maximum time to occlusion detection (h:mm:ss)**
Bolus Delivery		
3 units	0:01:00	0:01:35
25 units	0:01:05	0:01:25
Basal Delivery		
2.0 units/hour	1:01:39	1:29

2. Other Supportive Data Not Covered Above:

a. Hazard Analysis

A comprehensive hazard analysis for this device was reviewed in P180008 and P140015, in which design inputs and outputs, risks, and risk mitigations for hardware and software associated with proper functioning of the insulin pump component of those systems were reviewed in those PMA submission. The sponsor provided a revised hazard analysis in this submission to account for the unique design elements, intended use, and risks of the t:slim X2 insulin pump with interoperable technology which had not been previously reviewed. In particular, this revised hazard analysis accounted for the risks associated with interoperability between the device and other third party digital devices which met predefined criteria but were not specifically identified, including scenarios in which the device was put into an environment in which both compatible and incompatible digital devices attempted to communicate with the device and deliver commands. This analysis identified hazards which could

reasonably be anticipated to impact the proper use of the device, traced all identified risks to adequate design controls, and demonstrated that design features were appropriately implemented and validated.

b. Human Factors:

Human Factors validation tests were conducted with the pump, as well for the pump when connected to a representative digitally connected device. The Human Factors validation test was a nonrandomized, multicenter study that was performed using the device and thirty representative participants interacting with the device in a simulated use environment. An additional study of thirty-six representative participants ages 6-11 were conducted in a separate Validation Test. All study participants received training that was consistent with the training that patients would receive with the commercial product. Usability evaluations assessed comprehension and usability of the device for critical device tasks; results of the studies demonstrated that the pump could be safely used by intended users in the intended use environment when used alone and in combination with a digitally connected device.

c. Biocompatibility:

The t:slim X2 insulin pump with interoperable technology insulin cartridge was tested for biocompatibility in accordance with International Standard ISO-10993-1 as an external device with a duration of patient tissue contact of greater than twenty four hours to thirty days. The table below (Table 9) summarizes the biocompatibility testing conducted on the cartridge and the results of that testing.

Table 9: 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

d. Sterility:

A gamma sterilization process is used to sterilize the 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 insulin cartridge consistently achieve a sterility assurance level of 10-6.

The sponsor conducted packaging validation testing demonstrating that the specifications and integrity of the packaging system are maintained following sterilization and under environmental conditioning, distribution simulation, and accelerated and real time aging conditions for up to (b) (4) . The sterilization validation information provided for the disposable insulin cartridge for use in the pump supports the sterilization method and packaging with shelf life of (b) (4) when stored between -4°F and 140°F (-20°C to 60°C) and 20% to 90% relative humidity.

e. Insulin Compatibility and Stability:

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

f. Mechanical Engineering:

The t:slim X2 insulin pump with interoperable technology uses the same pump hardware as the insulin pump component of the systems approved in P180008 and P140015. Therefore, mechanical engineering testing provided and reviewed in P140015 and P180008 is applicable to this device. This includes information regarding performance testing, stress testing, reliability testing, packaging testing, shelf life testing, and storage testing performed in support of P180008 and P140015 to demonstrate the mechanical function of the device. System level testing mechanical testing (Performance, Environmental/Operational, and System Level Packaging/Shipping) was also conducted in those submissions and is similarly applicable to this device. Protocols, test reports, results, and acceptance criteria (as applicable) were provided in PMAs P180008 and P140015 and reviewed here and found to be acceptable to support the new intended use of this device. Testing performed is summarized in Table 10 below:

Table 10: Mechanical Testing Summary

Test	Purpose
Pump Environmental Storage testing	Determine pump performance after storage under reasonably anticipated environmental conditions
Drop Resistance testing	Determine compliance to pump specification regarding drop resistance
Fluid Ingress per IPX7	Determine pump reliability when exposed to water
Battery Verification	Determine battery life after 4 years of simulated depletion and

Test	Purpose
	recharging conditions
Random Vibration test (per IEC 60601-1-11)	Determine pump reliability under home use vibration conditions
Mechanical Shock (per IEC 60601-1-11)	Determine pump reliability under home use mechanical shock conditions
Vibrator Motor Testing	Confirm whether vibrator motor functions per specifications
Cartridge Push Test	Determine whether device meets product specifications regarding push test
Wake button cycling	Determine reliability of t:slim pumps after 4 years of simulated use
Motor Gear box cycling	Determine reliability of pumps after 4 years of simulated use
Occlusion Detection Test	Determine the ability of pump to detect relevant hazards associated with drug delivery and route of administration (the presence of an occlusion at minimum basal rate, intermediate basal rate and bolus.)
Bolus Delivery Time	Determine whether boluses are delivered in timeframes within product specification
Cartridge Detection	Determine the pump's cartridge detection time.
Cartridge Volume	Determine pump's compliance to insulin volume estimation requirements
Self Priming	Evaluate pump's self-priming capability.
Pump-Infusion Site Height Differential	Evaluate pump's ability to prevent unintentional flow under reasonably expected use conditions (flow due to 90 cm infusion site height differential
Pump Operating Temperature and Humidity	Evaluate pump's delivery accuracy over reasonably anticipated use conditions.
Pump Operating Pressure	Evaluate pump's delivery accuracy delivery over reasonably anticipated use conditions.
Alarm Pressure Level Test	Evaluate pump's ability to generate auditory alarms of adequate volume to notify user.
Operational Range (distance)	Determine compliance with product specifications regarding operational range.
Pump History	Determine compliance with product specifications regarding data logging ability of device to record critical events.
Cleaning Capability	Determine pump reliability after external cleaning.
Cartridge Installation Cycling	Determine pump reliability after 4 years of simulated use.

g. Electromagnetic Compatibility and Wireless Coexistence:

Electromagnetic compatibility (EMC), electromagnetic immunity (EMI) and wireless coexistence testing was performed for the t:slim Insulin Pump in compliance with

IEC 60601-1-2. The device passed all required testing with appropriate acceptance criteria and no deviations.

Radiofrequency (RF) communication testing was performed and demonstrated compliance with Federal Communications Commission standards (Title 47 Part 15). Radiated Emissions Test, Occupied Bandwidth, and Band-edge Measurement testing was performed. All tests were passed.

Radiofrequency wireless testing was conducted, including wireless coexistence. Testing demonstrated that the device can operate in the presence of RF interference and co-exists with other wireless devices operating in the same vicinity. The pump has been verified to communicate with a digitally connected device at its specified maximum distance of 20 feet . All tests passed.

h. Electrical Safety and Essential Performance:

The sponsor demonstrated testing for safety requirements for electrical equipment t:slim X2 insulin pump with interoperable technology in compliance with IEC 61010-1 (edition 3), including compliance with the following collateral standards:, IEC 60601-1-8, IEC 60601-1-11, IEC 60601-2-24. All tests passed acceptance criteria.

i. Packaging Integrity/Shipping Integrity:

The 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.

j. Data Logging:

The sponsor provided validated software protocols which enable the device to record critical events, including insulin delivery, pump commands and confirmations, connectivity states, malfunctions, alarms. These were reviewed and found to be adequate.

k. Interoperability:

A plan and approach for interoperability were provided according to the FDA Guidance *"Design Considerations and Pre-market Submission Recommendations for Interoperable Medical Devices - Guidance for Industry and Food and Drug*

Administration Staff" and determined to be adequate to support and clearly specify expectations, requirements, and interface specifications to potential interoperable devices. In addition, their plan covered their approach to working with connected device companies regarding contractual approaches, interfaces for data communication and exchange, and post-market reporting procedures and responsibilities (e.g., who is responsible for investigating and reporting complaints, malfunctions, and adverse events).

The sponsor additionally provided validated software protocols intended to ensure secure, accurate, and reliable communication with digital interfacing devices, as well as failsafe design features to mitigate the risks associated with interruption of communication with digitally connected devices. These protocols were reviewed and found to be adequate.

l. Cyber Security: Detailed information on cybersecurity of the device was reviewed and found to be acceptable.

J. Proposed Labeling:

The labeling supports the decision to grant the De Novo request for this device.

K. Identified Risks to Health and Mitigations Measures

Identified Risk	Mitigation Measures
Patient harm due to inadequate drug delivery accuracy that leads to over infusion or under infusion of drug.	Basal and bolus drug delivery accuracy validation testing Device use life reliability testing Design mitigations to prevent cross-channeling Validated and traceable risk control measures for identified hazards
Patient harm due to undetected pump occlusions that pose risk of under infusion of drug.	Hazard detection (e.g., drug occlusion) validation testing
Patient harm due to incompatibility between the drug and the pump that may lead to over infusion or under infusion of drug, or exposure to harmful substances leached from pump materials into the infused drug solution.	Drug compatibility testing

Identified Risk	Mitigation Measures
Inability to provide appropriate treatment due to loss of communication with digitally connected alternate pump controller devices.	Validated communication specifications, processes, and procedures with digitally connected devices
Commands from the digitally connected alternate pump controller devices that conflict with existing pump commands may lead to unintended over or under infusion of drug.	Validated communication specifications, processes, and procedures with digitally connected devices Validated failsafe design features
Conflicting interfaces resulting in over or under delivery.	Validated communication specifications, processes, and procedures with digitally connected devices Validated failsafe design features
Patient harm due to insecure transmission of data.	Validated communication specifications, processes, and procedures with digitally connected devices
Patient harm due to inability to determine source of dosing error when used in an integrated system.	Validated data logging capability
Patient harm due to exposure to hazardous and non-biocompatible materials or pathogens.	Biocompatibility testing Validation of reprocessing procedures
Patient harm due to data transmission interference/electromagnetic disturbance.	Electrical safety, electromagnetic compatibility, and radio frequency wireless safety testing
Patient harm due to incorrect use of pump, operational, and/or use-related errors.	Human Factors testing Transparent pump performance descriptions in labeling

L. Benefit/Risk Analysis

The t:slim X2 insulin pump with interoperable technology can function alone as an ambulatory insulin infusion pump as well as in conjunction with other digitally connected devices, including as part of an automated insulin dosing (AID) system.

The benefits of insulin pump therapy with continuous insulin infusion include the ability to administer insulin frequently without repeated injection; the ability to set different basal rates through the day to better match basal insulin requirements which may fluctuate during the course of the day; the ability to identify active insulin remaining from previous boluses to avoid “insulin stacking”, which can lead to hypoglycemia; and the ability to administer bolus doses over an extended time. The device is expected to provide general benefits of insulin pump therapy with continuous infusion. In addition to the general benefits of insulin pump therapy, the t:slim X2 insulin pump with interoperable technology pump can be used in

conjunction with digitally connected devices, and contribute to expected benefits associated with the specific devices with which it is connected. For example, when the device is incorporated into a system with a continuous glucose monitoring system (such as within an AID system), the user could experience the potential benefits associated with sensor augmented pump (SAP) therapy for example as described in the Summary of Safety and Effectiveness Data for P140015. The t:slim X2 insulin pump with interoperable technology pump could also be incorporated into a system with a AID controller algorithm. The use of this device in conjunction with an interoperable AID controller algorithm and a continuous glucose monitoring device could allow users to receive the benefits associated with closed loop insulin therapy, for example as described in the Summary of Safety and Effectiveness Data for P160017. The design of this device as enabled for external control is anticipated to facilitate innovation in digitally connecting compatible devices together to meet user needs, and is expected increase the safe and effective therapeutic choices commercially available to patients using insulin pump therapy.

The uncertainty of the benefits and the risks associated with the use of this device is reduced by the special controls including requirements for device design, which includes predetermined communication specifications and validation plans that potential interoperable devices must meet before this device may be used in a combination with those components. It is additionally reduced by device labeling, which clearly describes pump performance parameters, so that developers of potential connected devices (including AID algorithms) may determine whether this device is capable of meeting the needs of any potential system which might incorporate it as an interoperable component. The interoperability plans incorporated into the design of this insulin pump, which serves to define the requirements for devices it would be interoperable with, sufficiently addresses these uncertainties and adequately assures that the uncertainty related to anticipated benefits is acceptable for its intended use and intended use population.

There are several general risks associated with the use of this insulin pump, which include:

- Hypoglycemia from over-delivery of insulin due to a pump defect
- Cessation of or decreased insulin delivery resulting in hyperglycemia and possibly DKA due to pump failure, problems with the cannula or insulin infusion set tubing catheter occlusion, dislodgement, or fracture during infusion set insertion resulting in injury and/or inability to administer insulin
- Mechanical or battery failures resulting in interruptions in insulin delivery or incorrect insulin delivery
- Skin irritation, or redness, inflammation, pain or discomfort, bruising, edema, rash bleeding, infection, or allergic reaction at the infusion site
- Failure of the infusion set or complications at the infusion site, e.g. lipohypertrophy from repeatedly using the same site, resulting in inability to administer insulin or the variability of insulin absorption at the site.
- Use of an incompatible drug leading to over infusion or under infusion or exposure to harmful substances.
- Patient harm due to incorrect use of the pump (operational and/or use related errors)

These risks are mitigated by the special controls for this device including device design requirements, and the validation of certain specifications through non-clinical testing provided by the sponsor.

In addition to the risks above, when the device is used in conjunction with other interoperable digital devices, the risks associated with the device include:

- Inability to provide appropriate treatment due to loss of communication with digitally connected devices, including AID systems or external pump controller devices, and subsequent lack of data transmission
- Patient harm due to insecure transmission of data
- Patient harm due to data transmission interference and/or electromagnetic disturbances
- Risks of over or under doing insulin if the pump does not revert to a safe state (profile basal) when connection to a controlling external device is lost
- Risks of over or under doing insulin if the pump allows external control by more than one input device at the same time.

These risks are mitigated by the special controls for this device including device design requirements, and the validation of certain specifications through testing provided by the sponsor.

Overall, the probable benefits of the t:slim X2 insulin pump with interoperable technology outweigh the probable risks for the proposed indications for use in light of the special controls for this type of device and in combination with the general controls.

Patient Perspectives

Patient perspectives considered include information provided directly to the Agency by patients in written statements and also obtained through discussion with patients and patient advocacy groups at public forums regarding patient experiences with insulin pumps and digitally connected diabetes devices. This device will allow patients, in conjunction with their healthcare providers, to have more choice in the insulin pump that integrates with other elements of their diabetes management strategy and works best for their body and their care. In addition, availability of this device will facilitate agile technology development that will ultimately provide innovative diabetes diagnostics and therapies to patients more quickly.

M. Conclusion

The information provided in this *de novo* submission is sufficient to classify this device into class II under regulation 21 CFR 880.5730. FDA believes that special controls, along with general controls, provide reasonable assurance of the safety and effectiveness of this device type. The device is classified under the following:

Product Code: QFG
Device Type: Alternate controller enabled infusion pump
Class: II (special controls)
Regulation: 21 CFR 880.5730

(a) *Identification.* An alternate controller enabled infusion pump (ACE pump) is a device intended for the infusion of drugs into a patient. The ACE pump may include basal and bolus drug delivery at set or variable rates. ACE pumps are designed to reliably and securely communicate with external devices, such as automated drug dosing systems, to allow drug delivery commands to be received, executed, and confirmed. ACE pumps are intended to be used both alone and in conjunction with digitally connected medical devices for the purpose of drug delivery.

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b) *Classification.* Class II (special controls). Alternate controller enabled infusion pumps must comply with the following special controls:

1. Design verification and validation must include the following:
    a. Evidence demonstrating that device infusion delivery accuracy conforms to defined user needs and intended uses and is validated to support safe use under actual use conditions.
        i. Design input requirements must include delivery accuracy specifications under reasonably foreseeable use conditions, including ambient temperature changes, pressure changes (e.g., head-height, backpressure, atmospheric), and, as appropriate, different drug fluidic properties.
        ii. Test results must demonstrate that the device meets the design input requirements for delivery accuracy under use conditions for the programmable range of delivery rates and volumes. Testing shall be conducted with a statistically valid number of devices to account for variation between devices.
    b. Validation testing results demonstrating the ability of the pump to detect relevant hazards associated with drug delivery and the route of administration (e.g., occlusions, air in line, etc.) within a clinically relevant timeframe across the range of programmable drug delivery rates and volumes. Hazard detection must be appropriate for the intended use of the device and testing must validate appropriate performance under the conditions of use for the device.
    c. Validation testing results demonstrating compatibility with drugs which may be used with the pump based on its labeling. Testing must include assessment of drug stability under reasonably foreseeable use conditions which may affect drug stability (e.g., temperature, light exposure, or other factors as needed).
    d. The device parts that directly or indirectly contact the patient must be demonstrated to be biocompatible. This shall include chemical and particulate characterization on the final, finished, fluid contacting device components demonstrating that risk of harm from device-related residues is reasonably low.

e. Evidence verifying and validating that the device is reliable over the ACE pump use life, as specified in the design file, in terms of all device functions and in terms of pump performance.

f. The device must be designed and tested for electrical safety, electromagnetic compatibility, and radio frequency wireless safety and availability consistent with patient safety requirements in the intended use environment.

g. For any device that is capable of delivering more than one drug, the risk of cross-channeling drugs must be adequately mitigated.

h. For any devices intended for multiple patient use, testing must demonstrate validation of reprocessing procedures and include verification that the device meets all functional and performance requirements after reprocessing.

2. Design verification and validation activities must include appropriate design inputs and design outputs that are essential for the proper functioning of the device that have been documented and include the following:

   a. Risk control measures shall be implemented to address device system hazards and the design decisions related to how the risk control measures impact essential performance shall be documented.

   b. A traceability analysis demonstrating that all hazards are adequately controlled and that all controls have been validated in the final device design.

3. The device shall include validated interface specifications for digitally connected devices. These interface specifications shall, at a minimum, provide for the following:

   a. Secure authentication (pairing) to external devices.

   b. Secure, accurate, and reliable means of data transmission between the pump and connected devices.

   c. Sharing of necessary state information between the pump and any digitally connected alternate controllers (e.g., battery level, reservoir level, pump status, error conditions).

   d. Ensuring that the pump continues to operate safely when data is received in a manner outside the bounds of the parameters specified.

   e. A detailed process and procedure for sharing the pump interface specification with digitally connected devices and for validating the correct implementation of that protocol.

4. The device must include appropriate measures to ensure that safe therapy is maintained when communications with digitally connected alternate controller devices is interrupted, lost, or re-established after an interruption (e.g., reverting to a pre-programmed safe drug delivery rate). Validation testing results must demonstrate that critical events that occur during a loss of communications (e.g., commands, device malfunctions, occlusions, etc.) are handled appropriately during and after the interruption.

5. The device design must ensure that a record of critical events is stored and accessible for an adequate period to allow for auditing of communications between digitally connected devices, and to facilitate

the sharing of pertinent information with the responsible parties for those connected devices. Critical events to be stored by the system must, at a minimum, include:

a. A record of all drug delivery

b. Commands issued to the pump and pump confirmations

c. Device malfunctions

d. Alarms and alerts and associated acknowledgements

e. Connectivity events (e.g., establishment or loss of communications)

6. Design verification and validation must include results obtained through a human factors study that demonstrates that an intended user can safely use the device for its intended use.

7. Device labeling must include the following:

   a. A prominent statement identifying the drugs that are compatible with the device, including the identity and concentration of those drugs as appropriate.

   b. A description of the minimum and maximum basal rates, minimum and maximum bolus volumes, and the increment size for basal and bolus delivery, or other similarly applicable information about drug delivery parameters.

   c. A description of the pump accuracy at minimum, intermediate, and maximum bolus delivery volumes and the method(s) used to establish bolus delivery accuracy. For each bolus volume, pump accuracy shall be described in terms of the number of bolus doses measured to be within a given range as compared to the commanded volume. An acceptable accuracy description (depending on the drug delivered and bolus volume) may be provided as follows for each bolus volume tested, as applicable: number of bolus doses with volume that is <25%, 25% to <75%, 75% to <95%, 95% to <105%, 105% to <125%, 125% to <175%, 175 to 250%, and >250% of the commanded amount.

   d. A description of the pump accuracy at minimum, intermediate, and maximum basal delivery rates and the method(s) used to establish basal delivery accuracy. For each basal rate, pump accuracy shall be described in terms of the amount of drug delivered after the basal delivery was first commanded, without a warm-up period, up to various time points. The information provided must include typical pump performance, as well as worst-case pump performance observed during testing in terms of both over-delivery and under-delivery. An acceptable accuracy description (depending on the drug delivered) may be provided as follows, as applicable:

      i. The total volume delivered 1 hour, 6 hours, and 12 hours after starting delivery for a typical pump tested, as well as for the pump that delivered the least and the pump that delivered the most at each time point.

   e. A description of delivery hazard alarm performance, as applicable. For occlusion alarms, performance shall be reported at minimum, intermediate, and maximum delivery rates and volumes. This description must include the specification for the longest time period that may elapse before an occlusion alarm is triggered under each delivery condition, as well as the typical results observed during performance testing of the pumps.

f. For wireless connection enabled devices, a description of the wireless quality of service required for proper use of the device.

g. For any infusion pumps intended for multiple patient reuse, instructions for safely reprocessing the device between uses.