510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K241777

B Applicant

Insulet Corporation

C Proprietary and Established Names

SmartAdjust™ technology

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QJI	Class II	21 CFR 862.1356 – Interoperable Automated Glycemic Controller	CH – Clinical Chemistry

E Purpose for Submission:

Modification to a cleared device to expand the indications for use to include adults aged 18 years and older with type 2 diabetes mellitus.

II Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

SmartAdjust™ technology is intended for use with compatible integrated continuous glucose monitors (iCGM) and alternate controller enabled (ACE) pumps to automatically increase, decrease, and pause delivery of insulin based on current and predicted glucose values. SmartAdjust™ technology is intended for the management of type 1 diabetes mellitus in persons 2 years of age and older and type 2 diabetes mellitus in persons 18 years of age and older. SmartAdjust™ technology is intended for single patient use and requires a prescription.

C Special Conditions for Use Statement(s):

Rx – For Prescription Use Only

- SmartAdjust™ technology should not be used by anyone under the age of 2 years old.
- SmartAdjust™ technology should also NOT be used in people who require less than 5 units of insulin per day as the safety of the technology has not been evaluated in this population.
- Do not use SmartAdjust™ technology in pregnant women, critically ill patients, and those on dialysis. The safety of the SmartAdjust™ technology has not been evaluated in these populations.
- Do not use SmartAdjust™ technology if you are taking hydroxyurea as it could lead to falsely elevated CGM values and result in over-delivery of insulin that can lead to severe hypoglycemia.
- Do not use SmartAdjust™ technology if you do NOT have adequate hearing and/or vision to allow recognition of all functions of the Omnipod 5 System, including alerts, alarms, and reminders.
- SmartAdjust™ technology used with the Omnipod 5 System is designed to use rapid-acting U- 100 insulins. The following U-100 rapid-acting insulin analogs have been tested and found to be safe for use in the Pod: NovoLog® (insulin aspart), Humalog® (insulin lispro), and Admelog® (insulin lispro) for use up to 72 hours (3 days). Before using a different insulin with the Omnipod 5 System, check the insulin drug label and consult your healthcare provider. Refer to the insulin labeling and follow your healthcare provider's directions for how often to replace the Pod.
- SmartAdjust™ technology used with the Omnipod 5 System relies on accurate, current CGM values to determine your insulin needs. Always make sure you are using the CGM per manufacturer's instructions and do not extend the sensor wear beyond the recommended duration.
- Do NOT attempt to use the SmartAdjust™ technology with the Omnipod 5 System before you receive training. Inadequate training could put your health and safety at risk.
- Device components used with the SmartAdjust™ technology including the pod, CGM transmitter, and CGM sensor must be removed before Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, or diathermy treatment. In addition, the SmartAdjust™ Controller and smartphone should be placed outside of the procedure room. Exposure to MRI, CT, or diathermy treatment can damage the components.

III Device Description

SmartAdjust™ technology (the Omnipod 5 interoperable automated glycemic controller, iAGC) is a software-only medical device intended for the management of type 1 diabetes in people 2 years of age and older. With this submission, the sponsor intends to market the device to adults aged 18 years and older with type 2 diabetes as well. SmartAdjust™ technology is part of the Omnipod 5 System made of the following components:

- Omnipod 5 ACE Pump (pod) – product code QFG, most recently cleared under K231826
- SmartAdjust™ Technology – product code QJI, most recently cleared under K232741
- SmartBolus Calculator – product code QRX, most recently cleared under K231824

- Integrated continuous glucose monitor (iCGM) – cleared for use with Dexcom G6 and G7, and Abbott Freestyle Libre 2

The SmartAdjust™ technology software resides on the Omnipod 5 ACE Pump (the Omnipod 5 Pod and Omnipod 5 App). The iAGC software is responsible for controlling insulin delivery via compatible ACE Pump when the system is in Automated Mode. iCGM data is transmitted from the iCGM to the ACE Pump via Bluetooth Low Energy technology. The SmartAdjust™ Technology uses this transmitted iCGM data in its calculations. The SmartAdjust™ technology can be turned off, and the Omnipod 5 ACE Pump will operate in Manual Mode, which delivers insulin based on healthcare provider (HCP) or user-defined basal programs.

The SmartAdjust™ technology has three states of operation: Automated Mode, Automated: Limited, and Activity. In Automated Mode, the system calculates insulin delivery every 5 minutes based on the user-customizable glucose target (110–150 mg/dL). Automated: Limited is enabled when the SmartAdjust™ technology is not receiving data from a connected iCGM for 20 minutes or more and during sensor warm-up. While in Automated: Limited, the user will receive no more than pre-programmed basal insulin. When a valid glucose value is received from the iCGM, the SmartAdjust™ technology will resume delivery of insulin in full Automated Mode. Activity is a temporary mode which the user may select for various time durations during automated mode up to 24 hours. With Activity, the algorithm reduces insulin delivery and sets a temporary glucose target to 150 mg/dL. Activity is intended for use during periods when insulin sensitivity is expected to be higher, such as during exercise.

IV Substantial Equivalence Information:

A Predicate Device Name(s):

SmartAdjust™ technology

B Predicate 510(k) Number(s):

K232741

C Comparison with Predicate(s):

Device & Predicate Device(s):	K241777	K232741
Device Trade Name	SmartAdjust™ Technology	SmartAdjust™ Technology
General Device Characteristic Similarities		
Intended Use/Indications For Use	SmartAdjust™ Technology is intended for use with compatible integrated continuous glucose monitors (iCGM) and alternate	Same

	controller enabled (ACE) pumps to automatically increase, decrease, and pause delivery of insulin based on current and predicted glucose values. It is intended for single patient use and requires a prescription.	
General Device Characteristic Differences		
Intended Use Population	People with type 1 diabetes aged 2 years and older and people with type 2 diabetes aged 18 years and older	People with type 1 diabetes aged 2 years and older

V Standards/Guidance Documents Referenced:

- ANSI AAMI ISO 14971:2019
  Medical devices – Application of risk management to medical devices
- ANSI AAMI HE75:2009/(R)2018
  Human factors engineering – Design of medical devices
- ANSI AAMI IEC 623-1:2015+AMD1:2020 (Consolidated Text)
  Medical devices Part 1: Application of usability engineering to medical devices including Amendment 1
- ISO 14155 Third edition 2020-07
  Clinical investigation of medical devices for human subjects – Good clinical practice

VI Performance Characteristics:

A. Analytical Performance

The SmartAdjust™ technology is a software-only device, therefore analytical performance characteristics are not applicable.

B. Other Supportive Instrument Performance Characteristics Data

For the evaluation of the system in clinical studies, the SmartAdjust™ technology was installed on the OmniPod 5 ACE Pump (Pod) insulin pump with interoperable technology, which was paired with the Dexcom G6 integrated continuous glucose monitor (iCGM). Details on the performance characteristics of these devices can be found in public decision summaries for each device.

Summary of Clinical Testing:

The SECURE-T2D clinical study was conducted to evaluate the SmartAdjust™ Technology in adults aged 18 years and older with type 2 diabetes.

Study Feature	**Description**
Title	Safety and Efficacy of the OmniPod 5 Automated Insulin Delivery System in Adults with Type 2 Diabetes (SECURE-T2D)
Study Design	Single-arm, multicenter, prospective clinical study
Number of Sites	Twenty-one (21) sites in the United States
Population	343 subjects aged 18 years and older who had been diagnosed with type 2 diabetes were enrolled. 289 participants completed the study. Key Inclusion Criteria • Aged 18-75 years old • Diagnosed with T2D and on current insulin regimen for at least 3 months prior to screening • Hemoglobin A1c (HbA1c) < 12% at screening Key Exclusion Criteria • Use of an AID pump in automated mode within 3 months prior to screening • Episodes of severe hypoglycemia or diabetic ketoacidosis in the past 6 months The recruitment goal for this study was to enroll a heterogenous subject pool reflective of the intended patient population. The study is notable for diversity of age, BMI, race/ethnicity, education, and income level in the subjects. There was also a range of diabetes duration, non-insulin medication, HbA1c, total daily dose, and carb-counting knowledge.
Protocol Overview/Synopsis	The study consisted of two phases: 1. 14-day standard therapy phase (baseline) 2. 13 weeks treatment on the Omnipod 5 System with planned meal and exercise challenges For the standard therapy phase, current Dexcom G6 iCGM users could provide data from a 14-day period within the last 30 days. Non-Dexcom iCGM users wore a study iCGM, in blinded mode, to record glucose measurements over 14 days while subjects managed their diabetes at home per their usual routine and remained on their current multiple daily injection or pump therapy, and sensor, if applicable.

	After completion of the standard therapy phase, subjects were trained on the Omnipod 5 System and transitioned to the hybrid-closed loop (HCL) therapy phase. Subjects participated in various challenges during the study: 1. Target glucose challenge: 64 study participants utilized 3 different glucose targets for 3 days each (150 mg/dL, 140 mg/dL, and 130 mg/dL). 2. Meal challenge: All study participants completed 4 days of a meal challenge that consisted of a meal that was ≥60 g of carbohydrates. Subjects gave a meal bolus with that meal on days 1 and 3 and skipped a meal bolus on days 2 and 4, and CGM metrics were compared 4 hours post meal. 3. Exercise challenge: All study participants underwent 3 exercise sessions on 3 days. Exercise consisted of 1 hour of mild intensity exercise and 30 minutes of moderate intensity exercise. Subjects did not change their glucose target before exercising. Subjects who consumed a meal prior to exercise followed their normal meal bolus routine (i.e., meal boluses were not adjusted to account for exercise), and 93% did not consume a snack prior to exercise. CGM metrics were assessed during exercise, 2 hours after exercise, and overnight after exercise. As part of the study, subjects completed questionnaires to assess patient reported psychosocial outcomes: T2-Diabetes Distress Assessment System, Pittsburgh Sleep Quality Index, and the Hypoglycemia Confidence Scale.
Safety Results	There was 1 severe hypoglycemia event during the study period, which was attributed to a manual bolus request that was greater than necessary for the food that was consumed. The study algorithm stopped insulin delivery in the setting of a decreasing glucose an hour after the bolus was administered, but the subject still experienced a hypoglycemic event. The subject was able to correct this with oral carbohydrates. There were no other severe hypoglycemia or diabetic ketoacidosis events during the study. There were 14 serious adverse events not related or unlikely to be related to the study device or treatments.

Participant Demographics

	Standard Therapy N = 320*	Treatment Period N = 305
Age (yrs.)		
<30	5 (2%)	5 (2%)
30-<45	45 (14%)	43 (14%)
45-<65	181 (57%)	171 (56%)
≥65	89 (28%)	86 (28%)
Mean (SD)	57 (11)	57 (11)
Range	20 to 75	20 to 75
Sex – Female n (%)	185 (58%)	175 (57%)
Height[a] (cm) – Mean (sd)	169 (9)	169 (9)
Weight[a] (kg) – Mean (sd)	100 (23)	100 (23)
BMI[a] (kg/m^2)		
<30	88 (28%)	84 (28%)
30-<45	93 (29%)	88 (29%)
45-<65	73 (23%)	70 (23%)
≥65	66 (21%)	63 (21%)
Mean (SD)	35 (8)	35 (8)
Range	22 to 70	22 to 70
Race		
American Indian/Alaskan Native	5 (2%)	5 (2%)
Hispanic or Latino	3	3
Asian	5 (2%)	5 (2%)
Hispanic or Latino	0	0
Black/African-American	77 (24%)	72 (24%)
Hispanic or Latino	0	0
More than one race	3 (<1%)	3 (<1%)
Hispanic or Latino	0	0
Native Hawaiian/Other Pacific Islander	2 (<1%)	2 (<1%)
Hispanic or Latino	0	0
White	208 (65%)	198 (65%)
Hispanic or Latino	48	45
Unknown/Not Reported	20 (6%)	20 (7%)
Hispanic or Latino	18	18
Ethnicity		
Hispanic	69 (22%)	66 (22%)
Non-Hispanic	249 (78%)	237 (78%)
Unknown/not reported	2 (<1%)	2 (<1%)
Education		
< High School Diploma	20 (6%)	20 (7%)
High School Diploma	82 (26%)	79 (26%)
Technical/Vocational	17 (5%)	17 (6%)
Associate Degree	60 (19%)	56 (18%)
Bachelor's Degree	76 (24%)	70 (23%)
Advanced Degree	40 (13%)	40 (13%)
Do not wish to provide	25 (8%)	23 (8%)

Annual Household Income		
<$25,000	43 (13%)	42 (14%)
$25,000-<$35,000	27 (8%)	23 (8%)
$35,000-<$50,000	21 (7%)	19 (6%)
$50,000-<$75,000	49 (15%)	49 (16%)
$75,000-<$100,000	28 (9%)	26 (9%)
$100,00-<$200,000	54 (17%)	51 (17%)
$200,000 or more	16 (5%)	16 (5%)
Unknown	16 (5%)	16 (5%)
Does not wish to report	66 (21%)	63 (21%)
Health Insurance		
Private	170 (53%)	161 (53%)
Medicaid	28 (9%)	27 (9%)
Medicare	53 (17%)	52 (17%)
Other government	29 (9%)	27 (9%)
No coverage	18 (6%)	18 (6%)
No answer	22 (7%)	20 (7%)

[*]N = 343 enrolled; however, expect for age, data are missing for N = 23. Thus, this cohort includes N = 320.
[a]Values collected at Visit 4 (initiation of treatment period); all other values collected at Visit 1.

Participant Diabetes History

	Standard Therapy N = 320*	**Treatment Period N = 305**
Diabetes Duration (yrs.)		
<5	**18 (6%)**	**14 (5%)**
5-<10	**47 (15%)**	**46 (15%)**
10-<20	**132 (41%)**	**128 (42%)**
≥20	**123 (38%)**	**117 (38%)**
Median (IQR)	**17 (11, 24)**	**17 (11, 24)**
Range	**0.3 to 41**	**0.3 to 41**
Insulin Modality		
Pump	17 (5%)	17 (6%)
Injections	303 (95%)	288 (94%)
Insulin		
Basal/Bolus	252 (79%)	240 (79%)
Basal only	66 (21%)	63 (21%)
Pre-mix	2 (<1%)	2 (<1%)
Non-Insulin Glucose Lowering Medications of Interest[a] – n (%)		
GLP-1	178 (56%)	168 (55%)
SGLT2	143 (45%)	135 (44%)
DPP4	8 (3%)	8 (3%)
GLP1 or SGLT2[b]	145 (45%)	139 (46%)
GLP1 and SGLT2[b]	88 (28%)	82 (27%)

Prior Continuous Glucose Monitor Use		
Never	80 (25%)	75 (25%)
In past, but not current	44 (14%)	42 (14%)
Current	196 (61%)	188 (62%)
Duration of CGM use at Baseline		
<3 months	16 (8%)	16 (9%)
3-<6 months	20 (10%)	20 (11%)
6 months-<1 year	29 (15%)	27 (14%)
1-<2 years	46 (23%)	43 (23%)
2-<5 years	69 (35%)	67 (36%)
>=5 years	16 (8%)	15 (8%)
HbA1c – Local		
<8.0%	160 (50%)	152 (50%)
8.0%-<9.0%	76 (24%0	72 (24%)
≥9.0%	84 (26%)	81 (27%)
Mean (SD)	8.2 (1.4)	8.2 (1.4)
Range	4.9 to 11.9	4.9 to 11.9
Total Daily Insulin (U/kg/day)		
Mean (SD)	0.8 (0.5)	0.8 (0.5)
Range	0.1 to 2.9	0.1 to 2.9
Severe Events		
Severe hypoglycemia ever	14 (4%)	13 (4%)
Diabetic ketoacidosis ever	18 (6%)	16 (5%)
Hyperosmolar hyperglycemic state ever	1 (<1%)	1 (<1%)
c-Peptide[c,d] (nmol/L) – Median (IQR)	1.0 (0.6, 1.4)	1.0 (0.6, 1.4)
Serum Creatinine [c,e] (mg/dL) – Median (IQR)	0.9 (0.7, 1.1)	0.9 (0.7, 1.1)
GAD Antibody [c,f] (IU/mL) – n (%)		
<5.0	284 (93%)	284 (93%)
5.0< to <250	7 (2%)	7 (2%)
≥250	13 (4%)	13 (4%)

[*]N = 343 enrolled; however, except for age, data are missing for N = 23. Thus, this cohort includes N = 320.

[a]Not mutually exclusive. In the N=320 cohort, 88 are on both SGLT2 and GLP1, 3 on both SGLT2 and DPP4, 2 on GLP1 and DPP4, and 1 on all 3. In the N=305 cohort, 82 are on both SGLT2 and GLP1, 3 on both SGLT2 and DPP4, 2 on GLP1 and DPP4, and 1 on all 3.

[b]Participants were enrolled with a goal of at least 20% on SGLT or GLP1 and at least 5% on both SGLT and GLP1.

[c]Values collected at Visit 4.

[d]Collected at Visit 4 only and missing for 5 participants.

[e]Collected at Visit 4 only and missing for 3 participants.

[f]Collected at Visit 4 only and missing for 1 participant.

Observed Results

The primary endpoint was the change in HbA1c from baseline (8.2%) to the end of 13 weeks of Omnipod 5 System use (7.4%). There was a mean change in HbA1c of –0.8% (P<0.001), with a larger change in mean HbA1c for those with a higher baseline HbA1c. The table below shows the results of the primary safety and efficacy endpoints across the entire study population:

	Baseline N = 296	**End of Study N = 296**	**Mean Estimate and 95% CI for End of Study vs. Baseline N = 296**	**P-value for End of Study vs. Baseline (non-inferiority)**
HbA1c[a] mean (SD)	8.2% (1.3%)	7.4% (0.9%)	-0.8% (-1.0%, -0.7%)	<0.001 [a,b]

[a]*Testing for non-inferiority with a NI limit of 0.3%.*

[b]*A sensitivity analysis was done using Rubin's multiple imputation for the N=9 participants who dropped out without a 13-week HbA1c value. This gave the same point estimate, confidence interval and p-value as above: -0.8% (-1.0%, -0.7%); p<0.001. Note, any HbA1c measurements outside the analysis window of 42-119 days (6-17 weeks) from AID initiation were treated as missing data.*

There was no statistically significant change in HbA1c between sex, income or education level, or other medication use. There was a significant change in HbA1c between different age, race/ethnicity, pre-study carb counting knowledge, and baseline HbA1c. Specifically, the most improvement in HbA1c was noted in Hispanic or other subjects, subject ages 31-45 years old, and subjects who did not carb count prior to this study. Finally, subjects with the highest starting baseline (HbA1c ≥ 9%) had the greatest improvement in HbA1c from a mean of 10.1% to 8.1%. The table below shows subgroup analyses for the change in HbA1c by baseline characteristics:

	Standard Therapy	**Treatment Period**	**Difference**	**Interaction P-Value***
Gender				
Female (N = 168)				0.73/0.54
Mean ± SD	8.3 ± 1.4	7.4 ± 0.9	-0.9 ± 1.1	
[Range]	4.9 to 11.7	5.6 to 9.8	-5.3 to 1.2	
Male (N = 128)				
Mean ± SD	8.1 ± 1.2	7.3 ± 0.8	-0.8 ± 1.0	
[Range]	6.2 to 12.0	5.7 to 10.6	-5.1 to 2.8	
Race/Ethnicity				
Non-Hispanic White (N = 148)				0.03/0.004
Mean ± SD	7.9 ± 1.1	7.2 ± 0.8	-0.7 ± 0.9	
[Range]	5.5 to 11.1	5.6 to 10.6	-3.7 to 2.8	
Non-Hispanic Black/African-American (N = 69)				
Mean ± SD	8.6 ± 1.4	7.8 ± 1.0	-0.8 ± 1.0	
[Range]	5.3 to 12.0	5.6 to 9.8	-3.4 to 1.2	
Latino(x)/Hispanic (N = 65)				
Mean ± SD	8.5 ± 1.5	7.4 ± 0.9	-1.2 ± 1.2	

[Range]	4.9 to 11.9	5.7 to 9.5	-5.3 to 0.8	
Other (N = 14)				
Mean	8.5 ± 1.4	7.3 ± 0.9	-1.2 ± 1.2	
[Range]	7.0 to 11.7	6.3 to 9.3	-4.2 to 0.6	
Age				
18-<30 years (N = 5)				
Mean ± SD	7.5 ± 2.3	7.2 ± 1.5	-0.2 ± 0.8	
Range	4.9 to 11.1	5.7 to 9.8	-1.3 to 0.8	
30-<45 years (N = 41)				
Mean ± SD	8.8 ± 1.6	7.4 ± 1.0	-1.4 ± 1.3	
Range	5.3 to 11.7	5.6 to 9.5	-5.3 to 0.6	0.006/0.51
45-<65 years (N = 166)				
Mean ± SD	8.3 ± 1.2	7.4 ± 0.9	-0.8 ± 1.0	
Range	6.2 to 12.0	5.6 to 10.6	-3.4 to 2.8	
≥ 65 years (N = 84)				
Mean ± SD	7.9 ± 1.1	7.2 ± 0.8	-0.6 ± 0.9	
Range	5.5 to 11.0	5.7 to 9.1	-5.1 to 0.9	
Income				
<$50,000/year (N = 81)				
Mean	8.5 ± 1.5	7.6 ± 1.0	-0.9 ± 1.0	
[Range]	5.3 to 11.3	5.6 to 9.8	-5.1 to 1.2	
$50,000 -<$100,000/year (N = 72)				
Mean	8.1 ± 1.2	7.2 ± 0.7	0.9 ± 1.1	
[Range]	5.5 to 12.0	5.6 to 9.8	-5.3 to 0.9	
$100,000-<$200,000/year (N = 51)				0.80/0.54
Mean	8.0 ± 1.0	7.3 ± 0.8	-0.7 ± 0.9	
[Range]	6.8 to 11.7	5.8 to 9.7	-3.4 to 0.7	
≥$200,000/year (N = 16)				
Mean	8.3 ± 1.6	7.3 ± 0.8	-1.0 ± 1.3	
[Range]	6.2 to 11.6	5.9 to 9.0	-4.2 to 0.4	
Unknown (N = 76)				
Mean	8.2 ± 1.3	7.4 ± 1.0	-0.8 ± 1.1	
[Range]	4.9 to 11.9	5.7 to 10.6	-3.7 to 2.8	
Education				
High School/GED or Less (N = 95)				
Mean ± SD	8.4 ± 1.3	7.4 ± 1.0	-1.0 ± 1.0	
[Range]	6.2 to 12.0	5.6 to 10.6	-3.4 to 2.8	
Technical/Vocational/Associates (N = 70)				0.72/0.18
Mean ± SD	7.9 ± 1.3	7.1 ± 0.7	-0.9 ± 1.1	
[Range]	4.9 to 11.3	5.6 to 8.5	-5.3 to 0.9	
College Degree (N = 70)				
Mean ± SD	8.3 ± 1.3	7.6 ± 0.9	-0.7 ± 1.0	
[Range]	6.2 to 11.9	5.9 to 9.8	-5.1 to 1.0	
Advanced Degree (N = 40)				

Mean ± SD [Range]	8.1 ± 1.4 6.0 to 11.7	7.3 ± 0.9 5.9 to 9.3	-0.8 ± 1.1 -4.2 to 0.6	
Do not wish to provide (N = 21) Mean ± SD [Range]	8.3 ± 1.3 6.2 to 10.7	7.5 ± 0.9 6.0 to 9.8	-0.8 ± 1.1 -3.7 to 1.1	
Insurance				
Private (N = 159) Mean ± SG [Range]	8.1 ± 1.3 4.9 to 12.0	7.3 ± 0.9 5.6 to 9.8	-0.8 ± 1.0 -5.3 to 1.1	0.50/0.69
Other (N = 101) Mean ± SG [Range]	8.2 ± 1.4 5.5 to 11.9	7.4 ± 1.0 5.8 to 10.6	-0.8 ± 1.1 -5.1 to 2.8	
No coverage (N = 18) Mean ± SG [Range]	9.1 ± 1.3 6.7 to 10.6	7.9 ± 0.8 5.7 to 9.0	-1.2 ± 1.1 -2.8 to 1.0	
No answer (N = 18) Mean ± SG [Range]	8.4 ± 1.4 6.2 to 10.7	7.4 ± 0.7 6.0 to 9.1	-0.9 ± 1.1 -3.7 to 0.4	
Pre-Study Carb Counting (excludes basal-only users)				
Carb Counting (N = 49) Mean ± SD [Range]	7.6 ± 1.0 5.5 to 11.7	7.2 ± 1.0 5.8 to 10.6	-0.4 ± 0.9 -2.4 to 2.8	0.02/0.60
Fixed Dose (N = 108) Mean ± SD [Range]	8.3 ± 1.4 5.3 to 11.6	7.4 ± 0.9 5.6 to 9.8	-0.9 ± 1.1 -5.1 to 1.0	
Sliding Scale (N = 46) Mean ± SD [Range]	8.1 ± 1.4 4.9 to 12.0	7.3 ± 0.8 5.6 to 8.9	-0.8 ± 1.0 -3.4 to 0.8	
Small/Medium/Large (N = 30) Mean ± SD [Range]	8.2 ± 1.4 6.2 to 11.9	7.3 ± 0.9 5.7 to 9.4	-0.9 ± 0.9 -2.7 to 0.4	
Other (N = 1) Mean ± SD [Range]	NA NA	NA NA	NA NA	
C-Peptide				
<0.5 (N = 50) Mean ± SD [Range]	8.2 ± 1.3 6.2 to 11.3	7.4 ± 0.8 5.7 to 9.6	-0.8 ± 1.0 -3.7 to 0.6	0.67/0.54
0.5-<1.0 (N = 105) Mean ± SD [Range]	8.2 ± 1.5 4.9 to 11.7	7.4 ± 0.9 5.6 to 9.8	-0.8 ± 1.1 -5.3 to 1.0	
1.0-<1.5 (N = 75) Mean ± SD [Range]	8.3 ± 1.2 6.3 to 11.9	7.3 ± 0.9 5.7 to 9.7	-1.0 ± 0.9 -5.1 to 0.6	
≥1.5 (N = 61) Mean ± SD [Range]	8.1 ± 1.3 5.3 to 12.0	7.3 ± 1.0 5.6 to 10.6	-0.8 ± 1.1 -3.5 to 2.8	

Missing (N = 5) Mean ± SD [Range]	 8.5 ± 0.3 8.2 to 8.9	 7.8 ± 0.4 7.4 to 8.3	 -0.7 ± 0.5 -1.2 to -0.2	
SGLT2				
Yes (N = 130) Mean ± SD [Range]	 8.2 ± 1.3 5.5 to 12.0	 7.4 ± 0.9 5.7 to 10.6	 -0.8 ± 1.1 -4.2 to 2.8	0.50/0.54
No (N = 166) Mean ± SD [Range]	 8.3 ± 1.4 4.9 to 11.9	 7.4 ± 0.9 5.6 to 9.8	 -0.9 ± 1.0 -53 to 0.8	
GLP1				
Yes (N = 164) Mean ± SD [Range]	 8.1 ± 1.2 5.3 to 11.9	 7.3 ± 0.8 5.6 to 9.7	 -0.8 ± 1.0 -5.3 to 1.2	0.50/0.51
No (N = 132) Mean ± SD [Range]	 8.4 ± 1.4 4.9 to 12.0	 7.5 ± 1.0 5.6 to 10.6	 -0.9 ± 1.1 -5.1 to 2.8	
DDP4				
Yes (N = 8) Mean ± SD [Range]	 7.7 ± 1.4 6.2 to 10.8	 7.4 ± 0.8 5.9 to 8.3	 -0.4 ± 1.0 -2.5 to 0.7	0.33/0.54
No (N = 288) Mean ± SD [Range]	 8.2 ± 1.3 4.9 to 12.0	 7.4 ± 0.9 5.6 to 10.6	 -0.9 ± 1.0 -5.3 to 2.8	
≥1 Agent				
Yes (N = 219) Mean ± SD [Range]	 8.2 ± 1.3 5.3 to 12.0	 7.3 ± 0.9 5.6 to 10.6	 -0.8 ± 1.0 -5.3 to 2.8	0.50/0.60
No (N = 77) Mean ± SD [Range]	 8.4 ± 1.4 4.9 to 11.7	 7.5 ± 0.9 5.6 to 9.8	 -0.9 ± 1.0 -5.1 to 0.8	
Baseline HbA1c (%)				
<7.0% (N = 42) Mean ± SD [Range]	 6.5 ± 0.4 4.9 to 6.9	 6.5 ± 0.6 5.6 to 7.7	 -0.0 ± 0.5 -1.2 to 1.0	<0.001/NA
7.0-7.9% (N = 104) Mean ± SD [Range]	 7.5 ± 0.3 7.0 to 7.9	 7.1 ± 0.6 5.8 to 10.6	 -0.4 ± 0.6 -2.0 to 2.8	
8.0-8.9% (N = 82) Mean ± SD [Range]	 8.5 ± 0.3 8.0 to 8.9	 7.6 ± 0.8 6.0 to 9.8	 -0.8 ± 0.7 -2.5 to 1.1	
≥9.0% (N = 68) Mean ± SD [Range]	 10.1 ± 0.9 9.0 to 12.0	 8.1 ± 0.9 5.9 to 9.8	 -2.1 ± 1.0 -5.3 to 0.0	

[*] *P-values compare the change in outcome between the characteristic levels. The first P-value is without adjusting for baseline outcome and the second P-value is with adjusting for baseline outcome.*

Key secondary endpoints of the study included mean glucose and percent time in range (70-180 mg/dL). There was a significant increase in the time in range from 45% to 66% and improvement in the time above range (>250 mg/dL) from 20% to 7%. There was an increase in the time below range (<54 mg/dL) from 0.01% to 0.04%. The table below shows the hierarchical CGM metrics and patient reported outcomes for the entire study population:

	Standard Therapy (N = 299)*	**Treatment Period (N = 299) ***	**Change in CGM Metrics**
Glucose Hours-Median (IQR)	336 (319, 336)	1921 (1736, 2016)	-
Mean glucose (mg/dL)			
Mean (SD)	202 (50)	170 (24)	-32 (39)
P-value	-	-	<0.001
(95% CI)	-	-	-32 (-37, -28)
% time 70-180 mg/dL			
Mean (SD)	45% (25%)	66% (17%)	20% (20%)
P-value	-	-	<0.001
(95% CI)	-	-	20% (18%, 22%)
% time 70-140 mg/dL			
Mean (SD)	21% (18%)	33% (17%)	12% (16%)
P-value	-	-	<0.001
(95% CI)	-	-	12% (10%, 13%)
% time ≥ 300 mg/dL			
Robust ^ Mean (SD)	7.9% (10.3%)	1.9% (2.4%)	-5.3% (7.9%)
P-value	-	-	<0.001
(95% CI)	-	-	-5.3% (-6.3%, -4.4%)
% time > 250 mg/dL			
Robust ^ Mean (SD)	20% (22%)	7% (8%)	-12% (17%)
P-value	-	-	<0.001
(95% CI)	-	-	-12% (-14%, -11%)
% time > 180 mg/dL			
Mean (SD)	54% (25%)	34% (17%)	-20% (20%)
P-value	-	-	<0.001
(95% CI)	-	-	-20% (-22%, -18%)
% time <70 mg/dL			
Robust ^ Mean (SD)	0.2% (0.3%)	0.2% (0.2%)	0.0% (0.03)
Non-inferiority P-value	-	-	<0.001
(NI margin = 2.0%)	-	-	
(95% CI)			0.0% (-0.1%, 0.0%
% time <54 mg/dL			
Robust ^ Mean (SD)	0.01% (0.02%)	0.04% (0.05%)	0.01% (0.05%)
Non-inferiority P-value	-	-	<0.001
(NI margin = 0.5%)	-	-	
(95% CI)			0.01% (0.00%, 0.01%)
T2-DDAS total intensity score †	N = 305	N = 301	N = 301
Mean (SD)	2.5 (1.0)	2.2 (0.9)	
P-value	-	-	-0.3 (0.9)

(95% CI)	-	-	<0.001
T2-DDAS total intensity score ≥2.0	201 (66%)	167 (55%)	-0.3 (00.4, -0.2)
P-value			<0.001
PSQI total score[†]	N = 304	N = 300	N = 294
Mean (SD)	7.3 (4.0)	7.0 (4.1)	-0.4 (2.9)
P-value	-	-	0.04
(95% CI)	-	-	-0.4 (-0.7, 0.0)
PSQI total score >5.0	190 (63%)	174 (59%)	
P-value			0.10
HCS total score	N = 305	N = 300	N = 300
Mean (SD)	3.2 (0.6)	3.3 (0.6)	0.1 (0.6)
P-value	-	-	NA[#]
(95% CI)	-	-	0.1 (0.0, 0.1)
HCS total score <3.0	98 (32%)	75 (25%)	
P-value			NA[#]
% time <70 mg/dL			
Robust [^] Mean (SD)	0.2% (0.3%)	0.2% (0.2%)	0.0% (0.03)
Superiority P-value	-	-	NA[#]
(95% CI)	-	-	0.0% (-0.1%, 0.0%)
% time <54 mg/dL			
Robust [^] Mean (SD)	0.01% (0.02%)	0.04% (0.05%)	0.01% (0.05%)
Superiority P-value	-	-	NA[#]
(95% CI)	-	-	0.01% (0.00%, 0.01%)
Coefficient of Variation			
Mean (SD)	27.8% (6.3%)	27.1% (5.1%)	-0.7% (5.6%)
P-value	-	-	NA[#]
(95% CI)	-	-	-0.7% (-1.4%, -.01%)

[*]*Based on the pre-specified criteria ("CGM analyses will include all participants with ≥168 hours of CGM data during each of the Standard therapy period and the 13-week treatment period."), N=299 for the glycemic metrics.*
[^]*Similar with medians, robust means do not add up; that is difference of medians is not the same as the median of the differences. On the other hand, standard means add up and thus any inconsistency noticed above is due to rounding.*
[†]*Lower scores indicate better outcomes (e.g., less stress/distress related to diabetes, better sleep quality).*
[#]*As part of the hierarchy testing and because of the p-value=0.10 for PSQI > 5 the formal testing stopped, and p-values were not given for any outcomes further down on the list.*

Challenge Results

During this clinical study, subjects participated in up to 3 different challenges. Sixty-four subjects participated in a target glucose challenge in which they utilized 3 different glucose targets for 3 days each (150 mg/dL, 140 mg/dL, and 130 mg/dL). The mean time in range was the highest in the 150 mg/dL target group (66%) and was lower in the two remaining target groups (63% in both). There was no significant difference in time above 180 mg/dL or 250 mg/dL between all three groups and there was a mean of 0% time below 70 mg/dL and 54 mg/dL in all three groups.

All subjects participated in the meal challenge which lasted 4 days and consisted of a meal that was ≥60 g of carbohydrates. Subjects gave a meal bolus on days 1 and 3 and skipped the meal bolus on days 2 and 4. CGM metrics were compared at 4 hours post meal. The mean time in range was elevated when given a bolus (55%) compared to without a bolus (44%). There was more time above range when the bolus was skipped, but no difference in time below range for the two different actions.

All subjects also participated in the exercise challenge in which they underwent 3 exercise sessions on 3 separate days. The exercise session consisted of 1 hour of mild intensity exercise and 30 minutes of moderate intensity exercise. Subjects did not change their glucose target, nor did they change their behavior for administering meal boluses prior to exercise if a meal was consumed, and 93% of them did not consume a snack prior to exercise. CGM metrics were assessed during exercise, 2 hours after exercise, and overnight after exercise. The mean time in range for all 3 timepoints was the same (73%) and time above 180 mg/dL was the same (27%). There was 0% time below 70 mg/dL and 54 mg/dL at all three timepoints. There was a slight increase in time above 250 mg/dL in the 2 hours post-exercise.

Summary of Human Factors Validation Study

Human Factors validation tests were conducted with the Omnipod 5 App installed on a compatible mobile device. A total of 1 feasibility study and 3 formative studies were conducted. This Human Factors program consisted of an iterative design process of prototyping, testing, analyzing, and refining the Omnipod 5 System for the type 2 diabetes indication. Following the 4 total preliminary studies, the final device design was evaluated in the summative study performed with 16 representative participants interacting with the device in a simulated use environment. All study participants received training that was consistent with the training that patients would receive with the commercial product. Usability evaluations assess comprehension and usability of the device for critical device tasks. Results of the study demonstrated that the device could be used safely by intended users in the intended use environment.

VII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

VIII Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.