



510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION DECISION SUMMARY

I Background Information:

A 510(k) Number

K251779

B Applicant

Insulet Corporation

C Proprietary and Established Names

Omnipod 5 algorithm

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

- Add 100 mg/dL as a target glucose value input to the algorithm.
- Modify the Automated Delivery Restricted (ADR) alert to allow users to remain in Automated Mode after acknowledging the Alert.

II Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Omnipod 5 algorithm 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. The Omnipod 5 algorithm 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. The Omnipod 5 algorithm is intended for single patient use and requires a prescription.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

- The Omnipod 5 algorithm should NOT be used by anyone under the age of 2 years old. The Omnipod 5 algorithm 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 The Omnipod 5 algorithm in pregnant women, critically ill patients, and those on dialysis. The safety of The Omnipod 5 algorithm has not been evaluated in these populations. Consult with your healthcare provider if any of these conditions apply to you before using The Omnipod 5 algorithm.
- DO NOT use the Omnipod 5 System if you do not have adequate vision and/or hearing to recognize all functions of the Omnipod 5 System including alerts, alarms, and reminders according to instructions.
- ONLY use rapid-acting U-100 NovoLog® (insulin aspart), Humalog® (insulin lispro), and Admelog® (insulin lispro) insulin in the Omnipod 5 System as they have been tested and found to be safe for use with this system. NovoLog, Humalog, and Admelog are compatible with the Omnipod 5 System for use up to 72 hours (3 days). Follow your healthcare provider's directions for how often to replace the Pod.
- AVOID administering insulin, such as by injection or inhalation, while wearing an active Pod as this could result in hypoglycemia. The Omnipod 5 System cannot track insulin that is administered outside of the system. Consult your healthcare provider about how long to wait after manually administering insulin before you start Automated Mode.
- AVOID changing your SmartBolus Calculator settings before consulting with your healthcare provider. Incorrect changes could result in over-delivery or under-delivery of insulin, which can lead to hypoglycemia or hyperglycemia. Settings that impact bolus calculations mainly include: Max Bolus, Minimum Glucose for Calculations, Correct Above, Correction Factor(s), Insulin to Carb (IC) ratio(s), Duration of Insulin Action, and Target Glucose.
- Do NOT use Omnipod 5 System with a Dexcom Sensor if you are taking hydroxyurea, a medication used in the treatment of diseases including cancer and sickle cell anemia. Your Dexcom sensor glucose values could be falsely elevated and could result in over-delivery of insulin which can lead to severe hypoglycemia.
- DO NOT use the Omnipod 5 System with the FreeStyle Libre 2 Plus Sensor if you are taking more than 1000 mg of ascorbic acid (Vitamin C) per day, a substance found in supplements like multivitamins or cold remedies such as Airborne® and Emergen-C®. Taking more than 1000 mg of Vitamin C per day may falsely raise your Sensor readings and result in over-delivery of insulin that could result in severe hypoglycemia.
- ALWAYS respond to Hazard Alarms as soon as they occur. Pod Hazard Alarms indicate that insulin delivery has stopped. Failure to respond to a Hazard Alarm could result in under-delivery of insulin which can lead to hyperglycemia.
- DO NOT use the Omnipod 5 System at low atmospheric pressure (below 700hPA). You could encounter such low atmospheric pressures at high elevations, such as when mountain climbing or living at elevations above 10,000 feet (3,000 meters). Change in atmospheric pressure can also occur during take-off with air travel. Unintended insulin delivery can occur if there is expansion of tiny air bubbles that may exist inside the Pod. This can result in hypoglycemia. It is important to check your glucose frequently when flying to avoid prolonged hypoglycemia.

- DO NOT use the Omnipod 5 System in oxygen rich environments (greater than 25% oxygen), which include home or surgical areas that use supplementary oxygen and hyperbaric chambers. Hyperbaric, or high pressure, chambers are sometimes used to promote healing of diabetic ulcers, or to treat carbon monoxide poisoning, certain bone and tissue infections, and decompression sickness. Exposure to oxygen rich environments could result in combustion of the Pod or Omnipod 5 Controller, which can cause severe burns to the body.
- DO NOT use the Omnipod 5 System in high atmospheric pressure environments (above 1060 hPA), which can be found in a hyperbaric chamber. Hyperbaric, or high pressure, chambers, are sometimes used to promote healing of diabetic ulcers, or to treat carbon monoxide poisoning, certain bone and tissue infections, and decompression sickness. Exposure to high atmospheric pressure environments can damage your Pod and Omnipod 5 Controller which could result in under-delivery of insulin which can lead to hyperglycemia.
- Device components including the Pod, Dexcom G6 Sensor and Transmitter, Dexcom G7 Sensor, and FreeStyle Libre 2 Plus Sensor must be removed before Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, or diathermy treatment. In addition, the Controller and smartphone should be placed outside of the procedure room. Exposure to MRI, CT, or diathermy treatment can damage the components.

III Device/System Characteristics:

The device is the Omnipod 5 (OP5) algorithm (formerly called the SmartAdjust technology), which is a software-only medical device and is part of the OP5 Automated Insulin Delivery System composed of the following devices:

- Omnipod 5 ACE Pump (Pod) initially cleared under K203768 and most recently cleared under K231826.
- Omnipod 5 Algorithm (iAGC) initially cleared under K203774 and most recently cleared under K241777.
- SmartBolus Calculator initially cleared under K203772 and most recently cleared under K231824).
- Third-party iCGM (cleared for use with Dexcom G6 and G7 and Abbott Freestyle Libre 2)

The OP5 algorithm (iAGC) calculates insulin micro-boluses every 5 minutes based upon the predicted glucose over a 60-minute prediction horizon. The OP5 algorithm can also provide autocorrection boluses in response to hyperglycemia.

The OP5 system is a hybrid closed loop system and can operate in either open loop (Manual Mode) or closed loop (Automated Mode). When Automated Mode is enabled, the OP5 algorithm controls insulin delivery based on recent iCGM values. Automated Mode has three states of operation: fully Automated, Automated: Limited (i.e., Limited Mode), and Activity.

- In fully Automated mode, the Algorithm calculates and adjusts insulin delivery based on several factors including the user's set glucose target, total daily insulin (TDI), and sensor glucose values.
- Limited Mode is enabled when the iAGC is not receiving data from a connected iCGM for 20 minutes or more. While in Limited Mode, the user will receive basal insulin at or below either the pre-programmed basal rate or the rate based on past insulin usage, whichever is less. Once the iAGC and iCGM are back into range and a valid EGV is

received from the iCGM, the system will resume delivery of insulin in fully Automated mode.

- Activity is intended for use during periods when insulin sensitivity is expected to be higher, such as during exercise. The feature can be set for various time durations during Automated mode. With Activity, the algorithm reduces insulin delivery by setting a temporary glucose target to 150 mg/dL. Activity has a maximum selectable duration of 24 hours.

IV Substantial Equivalence Information:

A Predicate Device Name(s):

SmartAdjust™ Technology

B Predicate 510(k) Number(s):

K241777

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K251779</u>	<u>K241777</u>
Device Trade Name	Omnipod 5 algorithm	SmartAdjust Technology
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Omnipod 5 algorithm 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. The Omnipod 5 algorithm 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. The Omnipod 5 algorithm is intended for single patient use and requires a prescription.	Same
General Device Characteristic Differences		

Target Glucose	100-150 mg/dl, user-customizable	110-150 mg/dl, user-customizable
Automated Delivery Restriction (ADR) Alert is triggered	2 hr after reaching the lower or upper bound constraint. User will be allowed to remain in the automated mode.	1 hr after reaching the lower or upper bound constraint. User will exit to manual mode.

V Standards/Guidance Documents Referenced:

- ANSI AAMI IEC 62304:2006/A1:2016 – Medical device software – Software life cycle processes
- ANSI AAMI ISO 14971:2019 – Medical devices – Applications of risk management to medical devices

VI Performance Characteristics (if/when applicable):

A Non-Clinical Performance:

There have been no changes to the Omnipod 5 algorithm's design, architecture, logical flows, or principles of operation from the predicate device cleared under K241777. For the changes proposed in this submission, software testing for the candidate device included unit testing, integration testing, design verification component-level testing, design system level testing, and design validation testing. All acceptance criteria have passed in these tests.

B Clinical Studies:

No new clinical studies were conducted to support substantial equivalence of the subject devices.

C Other Supportive Device Performance Characteristics Data:

Glycemic outcomes in people with diabetes using the Omnipod 5 Automated Insulin Delivery System with target glucose setting of 100 mg/dL was validated by a virtual clinical trial study using *in silico* simulations. This virtual clinical trial study used a multi-arm design to compare glycemic outcomes of digital twins at the new target glucose setting of 100 mg/dL with those of real-world users of the Omnipod 5 algorithm (also referred to as SmartAdjust technology) at target glucose settings of 110 mg/dL. The trial included 125 digital twins that were constructed using clinical data, including data from the Omnipod 5 pivotal study and other sources.

Information supporting credibility of the models used in the simulations was reviewed and found to be sufficient given the context of use. The following types of information, in addition to other information, were provided to support model credibility:

- Code verification was performed to verify the correct implementation of the simulator component models (e.g., iAGC, iCGM, and patient model).
- Details on the methods used for parameter optimization and training of digital twins was provided.

- Emergent model behavior: digital twins were tested to confirm physiologically correct glucose response to specific situations, including withholding of insulin, high insulin doses during fasting, and meals consumed without insulin.
- Population-based comparison of digital twin attributes (i.e., insulin therapy and physiological parameters) to those of the real world Omnipod 5 users.
- In vivo validation: as shown in the table below, the virtual cohort of digital twins were validated by matching the real-world data (RWD) of Omnipod 5 users with one target glucose setting (i.e., 130 mg/dL) after the digital twins were calibrated using RWD of Omnipod 5 users with other target glucose settings (i.e., 110 and 120 mg/dL). Statistical analysis using a two-sample t-test for the validation metric of difference in glycemic outcomes between the 130 mg/dL and 110 mg/dL setpoints (denoted as $\Delta(\text{SP130, SP110})$) indicates no statistically significant difference between simulated and real-world outcomes.

Metric $\Delta(\text{SP130, SP110})$	Simulated Outcomes	RWE Outcomes	p-value
% time in 70-180 mg/dL	-5.9 \pm 4.1	-5.6 \pm 8.8	0.7
% time above 180 mg/dL	6.5 \pm 3.9	6.0 \pm 9.1	0.6
% time below 70 mg/dL	-0.6 \pm 0.6	-0.4 \pm 1.1	0.1
Total daily insulin delivery (U)	-4.0 \pm 1.5	-4.0 \pm 10.5	1.0

The virtual clinical trial study and its results are summarized below:

- Virtual Trial Design
 - N=125 digital twins representing subjects with T1D aged 2 to 70 years
 - Age groups: 85 subjects ages >20 years, 18 subjects ages 13-19 years, 22 subjects ages 2-13 years
 - 72 simulation scenarios combining the following parameters:
 - Insulin needs: nominal therapy, more intense therapy than the need, less intense therapy than the need
 - Initial glucose level: 70, 110, 200, 250 mg/dL
 - Meal size: no meal, average meal, and large meal
 - Rescue carbohydrate behavior: triggered after 15 or 30 minutes of hypoglycemia
 - 12-hour simulation duration with 100 mg/dL target glucose value for each digital twin and each simulation scenario.

The results of the simulations were reviewed and found to be adequate to support a finding of substantial equivalence, as well as the applicable special controls required for interoperable automated glycemic controllers listed in 21 CFR 862.1356 (b)(1)(i). Virtual clinical trial results for primary outcomes (100 mg/dL in silico results vs 110 mg/dL real-world data) and age-specific safety profile are presented in tables 1 and 2 below, respectively.

The simulated clinical study showed numerical differences in times spent in different CGM glucose ranges for simulated subjects using the 100 mg/dL setpoint when compared to RWE

results for subjects using a 110 mg/dL setpoint. Specifically, the study showed reduced time above range, increased time in range, and increased time below range. These findings are consistent with the general trend observed in prior in vivo clinical studies of this device, where lowering the target glucose level reduces time above range, increases time in range, and increases time below range.

Table 1: Glycemic outcomes between Target Glucose 100 mg/dL (simulated) and 110 mg/dL (from RWE)

Endpoints	Target Glucose 100 mg/dL (Simulated), mean ± SD	Target Glucose 110 mg/dL (RWE), mean ± SD
% time in 70-180 mg/dL	65.9±12.2	63.4±13.7
% time > 180 mg/dL	32.3±12.9	35.1±14.2
% time < 70 mg/dL	1.8±1.6	1.5±1.5
% time < 54 mg/dL	0.5±0.8	0.3±0.5
Total daily insulin use (U)	49.4±18.3	46.9±21.5

Table 2: In silico simulation results for different age cohorts

	All	Adults	Adolescents	Pediatrics
Target Glucose 100 mg/dL (simulated)				
% time in 70-180 mg/dL	65.9±12.2	67.9±11.7	60.6±11.0	62.8±13.6
% time > 180 mg/dL	32.3±12.9	30.4±12.5	37.6±12.0	34.8±14.3
% time < 70 mg/dL	1.8±1.6	1.7±1.5	1.8±2.0	2.4±1.8
% time < 54 mg/dL	0.5±0.8	0.5±0.7	0.5±1.0	0.4±0.9
Total Daily Insulin (U)	49.4±18.3	49.3±18.2	59.1±12.5	41.0±19.6
Target Glucose 110 mg/dL (RWE)				
% time in 70-180 mg/dL	63.4±13.7	64.7±13.6	59.1±14.3	61.8±12.7
% time > 180 mg/dL	35.1±14.2	33.9±14.1	39.5±14.8	36.2±13.3
% time < 70 mg/dL	1.5±1.5	1.3±1.6	1.4±1.3	1.9±1.6
% time < 54 mg/dL	0.3±0.5	0.3±0.5	0.3±0.4	0.4±0.5
Total Daily Insulin (U)	46.9±21.5	47.1±21.2	56.2±19.3	38.9±21.0

The sponsor also estimated the 100 mg/dL setpoint outcomes using a complementary, statistical approach. RWE was collected from 32,332 device users of the 110, 120 and 130 mg/dL setpoints

(568 +/- 259 days). A statistical regression model (linear mixed effects) was fit to the characterize glycemic outcomes for these set points. This model was then used to extrapolate predictions of glycemic outcomes under a hypothetical 100 mg/dL setpoint. The results of this extrapolation are provided in Table 3 below.

Table 3: RWE extrapolation results for different age cohorts

	All	Adults	Adolescents	Pediatrics
% time in 70-180 mg/dl	66.3±12.4	68.2±12.2	61.2±12.8	63.3±11.3
% time > 180 mg/dl	32.0±12.8	30.3±12.7	37.2±13.2	34.5±11.7
% time < 70 mg/dl	1.7±1.2	1.6±1.2	1.6±1.1	2.2±1.3
Total Daily Insulin (U)	49.2±19.4	49.0±19.3	58.2±17.8	42.7±18.4

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.