Efficacy and safety of the Omnipod 5 System compared to pump therapy in the treatment of type 1 diabetes: a randomized, parallel-group clinical trial

Version 1.1

November 14, 2022

Insulet Corporation

100 Nagog Park

Acton, MA 01720

Protocol Approval

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Version 1.1

November 14, 2022

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Investigator Statement

Efficacy and safety of the Omnipod 5 System compared to pump therapy in the treatment of type 1 diabetes: a randomized, parallel-group clinical trial

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I agree to conduct the above referenced clinical study protocol in accordance with the design and specific provisions as designated in this protocol, the signed agreement with the Sponsor, all applicable regulatory requirements such as the Food and Drug Administration (FDA), Good Clinical Practice (GCP) and Declaration of Helsinki, and any conditions of approval imposed by an Institutional Review Board (IRB) or Ethics Committee (EC). Modifications to the study protocol are acceptable only in the form of a protocol amendment, except when necessary to protect the safety, rights, or welfare of participants. I agree to await Institutional Review Board (IRB) /Ethics Committees (EC) and Insulet approval for the protocol, informed consent and documentation to be presented to participants before initiating the study in accordance with ICH (International Conference on Harmonization)-GCP, obtain informed consent from participants prior to their enrollment into the study, to collect and record data as required by this protocol and case report forms, to report non serious and serious adverse events that may occur for any participant participating in this study under my care, to report product complaints for any of the devices utilized in this protocol, and to maintain study related documentation (regulatory documentation) for the period of time required. I agree to supervise all utilization of investigational study devices and to ensure their usage is only in connection with the Study. I agree to provide a Financial Disclosure Statement to Sponsor and will also notify Sponsor if my disclosed financial information changes during the Study and up to one year following the closure of the Study. I have read and understand the contents of this protocol. I agree to follow and abide by the requirements set forth in this document.

I understand the information in this document contains trade secrets and commercial information that are privileged or confidential and may not be disclosed unless such disclosure is required by applicable law or regulations. In any event, persons whom the information is disclosed must be informed that the information is privileged or confidential and may not be further disclosed by them. These restrictions on disclosure will apply equally to all future information supplied to me, which is indicated as privileged or confidential.

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Clinical Site Investigator Name (print)

_____ _____

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Protocol Summary

Protocol title	**Efficacy and safety of the Omnipod 5 System compared to pump therapy in the treatment of type 1 diabetes: a randomized, parallel-group clinical trial**
Protocol ID	OP5-003
Purpose	To demonstrate the efficacy and safety of the Omnipod 5 System compared to pump and continuous glucose monitor (CGM) therapy in adults with type 1 diabetes currently using pump therapy

Study Devices	The devices used in the Intervention group include:
	• Omnipod 5 System, comprised of the following components:
	  ○ Omnipod 5 Pod
	  ○ Omnipod 5 App (on the Insulet-provided Controller)
	• Dexcom G6 Continuous Glucose Monitor
	
	The devices used in the Control group include:
	• Participant's own insulin pump
	• Dexcom G6 Continuous Glucose Monitor

Primary objective	To demonstrate superior efficacy of the Omnipod 5 System compared to pump and CGM therapy in adults with type 1 diabetes
Secondary objective	To demonstrate additional measures of efficacy and safety of the Omnipod 5 System compared to pump and CGM therapy in adults with type 1 diabetes
Study Design	Adults with type 1 diabetes currently on pump therapy with an A1C between 7-11%, inclusive, will be recruited for the study. At least 80% of participants must have an A1C ≥ 8%. At least 50% of participants must be using Omnipod for pump therapy at the time of enrollment. Following a two-week standard therapy period where CGM data will be collected, participants will be randomized (2:1 ratio) to either: • Intervention Group – Omnipod 5 System with Dexcom G6 CGM or • Control Group – Participant's current insulin pump with Dexcom G6 CGM Both groups will participate for 13-weeks after completion of standard therapy. All participants will be required to use the study provided Dexcom G6 sensor for the duration of the study.
Primary Endpoint	The primary endpoint is per-participant percentage of time in range (TIR) 70-180 mg/dL as measured by study CGM and comparing the Intervention group to the Control group during the 13-week randomized period
Secondary Endpoints	The following secondary per-participant endpoints will be evaluated and compared in the Intervention group vs. Control group at the end of the 13-week randomized period:

	Secondary Endpoints: • Percentage of time <54 mg/dL (non-inferiority) • Percentage of time >180 mg/dL • Mean glucose • Change from baseline in A1C • Percentage of time < 70 mg/dL • Change from baseline in Type 1-Diabetes Distress Scale (T1-DDS) total score • Change from baseline in Hypoglycemia Confidence Scale (HCS) total score • Change from baseline in Diabetes Quality of Life-brief (DQOL-brief) total score
Exploratory Endpoints	The following exploratory endpoints will be evaluated and compared in the Intervention group vs. Control group at the end of the 13-week randomized period: • Proportion of participants with A1C <7% • Proportion of participants with A1C <8% • Proportion of participants with ≥1% improvement in A1C from baseline • Proportion of participants with ≥10 percentage point relative improvement in A1C from baseline • Proportion of participants with either ≥1% improvement in A1C from baseline OR ≥10 percentage point relative improvement in A1C from baseline • Change from baseline in Body Mass Index (BMI) • Change from baseline in total daily insulin (TDI) (units/kg) • Additional CGM-derived endpoints, such as coefficient of variation, time above range >250 mg/dL, percentage of time < 54 mg/dL (superiority), TIR during daytime and nighttime hours • Number of episodes of severe hypoglycemia • Number of episodes of DKA **Patient-Reported Outcomes:** The following questionnaires will be used to evaluate general and disease-specific quality of life, and device usability. Results will be assessed at 13 weeks compared to baseline (Intervention and Control group) • Clarke Hypoglycemia Awareness • EQ-5D-3L • Type 1 Diabetes Distress Scale (T1-DDS) • Diabetes Quality of Life-brief (DQOL-brief) • DAWN Impact of Diabetes Profile (DIDP) • Hypoglycemia Confidence Scale (HCS) • Pittsburgh Sleep Quality Index (PSQI) • System Usability Scale (SUS) • Insulin Dosing Systems: Perceptions, Ideas, Reflections, and Expectations (INSPIRE)

Eligibility Criteria	**Inclusion Criteria:** Participants must meet all the following criteria to be included in the study: 1. Age at time of consent 18-70 years of age 2. Diagnosed with type 1 diabetes for at least 1 year. Diagnosis is based on investigator's clinical judgment. 3. On pump therapy for ≥ 3 months prior to screening and familiar with pump therapy concepts such as basal and bolus insulin delivery, and carbohydrate counting. Participants using automated insulin delivery (AID) devices, including devices with predictive low glucose suspend (PLGS), in the 3 months prior to screening, will be excluded from participating. 4. A1C 7.0-11.0% by point-of-care taken at screening visit 5. Willing to use and obtain U-100 insulin: (either insulin aspart (Novolog, NovoRapid), or insulin lispro (Humalog, Admelog)), as the primary insulin treatment 6. Must have a smartphone that supports the Dexcom app download and participants must be willing to use the app throughout the study 7. Investigator has confidence that the participant can safely operate all study devices and can adhere to the protocol 8. Willing to wear the system continuously throughout the study 9. Willing and able to sign the Informed Consent Form (ICF) Exclusion Criteria: Participants who meet any of the following criteria will be excluded from the study: 1. Any medical condition, such as untreated malignancy, unstable cardiac disease, unstable or end-stage renal failure, eating disorders, or other conditions which in the opinion of the investigator, would put the participant at an unacceptable safety risk 2. History of severe hypoglycemia in the past 6 months 3. History of diabetic ketoacidosis (DKA) in the past 6 months, unrelated to an intercurrent illness or infusion set failure 4. Blood disorder or dyscrasia within 3 months prior to screening, including use of hydroxyurea, which in the investigator's opinion could interfere with determination of HbA1C. 5. Currently on systemic steroids or intends to receive systemic steroid treatment during study participation, including stable treatment for adrenal insufficiency. Inhaled, ophthalmic, topical, joint injection, and other locally applied steroids are allowed. 6. Unable to tolerate adhesive tape or has any unresolved skin condition in the area of sensor or pump placement 7. Use of non-insulin anti-hyperglycemic medication other than metformin, in the 12 weeks prior to the Baseline Visit. Participants taking metformin should remain on a steady dose during study participation. 8. Pregnant or lactating, or is a woman of childbearing potential and not on acceptable form of birth control (acceptable forms of contraception include abstinence, barrier methods such as condoms, hormonal contraceptives, intrauterine device, surgical

	sterilization such as tubal ligation or hysterectomy, or vasectomized partner) 9. Participation in another clinical study using an investigational drug or device within 30-days or 5 half-lives (whichever is longer) prior to screening, or intends to participate in any other study during this study period 10. Unable to follow clinical protocol for the duration of the study or is otherwise deemed unacceptable to participate in the study per the investigator's clinical judgment 11. Participant is an employee of Insulet, an Investigator or Investigator's study team, or immediate family member of any of the aforementioned
Sample Size	A total of up to 200 participants at up to 15 clinical sites across the United States (US) and France will be enrolled in the study, to obtain a minimum of 170 randomized participants.
Study Arms	Parallel-group 13-week randomized trial: • Intervention Group: Omnipod 5 System with Dexcom G6 CGM • Control Group: Participant's current insulin pump with Dexcom G6 CGM
Study Duration	The study is expected to be completed within 12-months which includes clinical site initiation to completion and all data entry and monitoring procedures. Each participant is expected to participate for approximately 15 weeks.
Device Indication Europe (EU) and United States (US)	**Europe:** The Omnipod 5® Automated Insulin Delivery System (Omnipod 5 System) is a single hormone insulin delivery system intended to deliver U-100 insulin subcutaneously for the management of type 1 diabetes in persons aged 2 and older requiring insulin. The Omnipod 5 System is intended to operate as an automated insulin delivery system when used with compatible CGM. When in Automated Mode, the Omnipod 5 System is designed to assist people with type 1 diabetes in achieving glycemic targets set by their healthcare providers. It is intended to modulate (increase, decrease or pause) insulin delivery to operate within predefined threshold values using current and predicted CGM values to maintain blood glucose at variable target glucose levels, thereby reducing glucose variability. This reduction in variability is intended to lead to a reduction in the frequency, severity, and duration of both hyperglycemia and hypoglycemia. The Omnipod 5 System can also operate in a manual mode that delivers insulin at set or manually adjusted rates. The Omnipod 5 System is intended for single patient use. The Omnipod 5 System is indicated for use with Novolog/NovoRapid, Humalog and Admelog U-100 insulin. **United States:**

	The Omnipod 5 Automated Insulin Delivery System in the US consists of 3 regulated devices. The indications for use for the 3 devices are as follows: The Omnipod 5 ACE (alternate controller enabled) Pump (Pod) is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The Omnipod 5 ACE 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 Omnipod 5 ACE Pump is intended for single patient, home use and requires a prescription. SmartAdjust™ technology is intended for use with compatible integrated continuous glucose monitors (iCGM) and 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 6 years of age and older. SmartAdjust technology is intended for single patient use and requires a prescription. The Omnipod 5 SmartBolus Calculator is software intended for the management of diabetes in persons aged 6 and older requiring rapid-acting U-100 insulin. The Omnipod 5 SmartBolus Calculator calculates a suggested bolus dose based on user-entered carbohydrates, most recent sensor glucose value (or blood glucose reading if using fingerstick), rate of change of the sensor glucose (if applicable), insulin on board (IOB), and programmable correction factor, insulin to carbohydrate ratio, and target glucose value. The Omnipod 5 SmartBolus Calculator is intended for single patient, home use and requires a prescription.

Glossary of Acronyms

ACE	Alternate Controller Enabled
ADA	American Diabetes Association
ADE	Adverse Device Effect
AE	Adverse Event
AID	Automated Insulin Delivery
ASADE	Anticipated Serious Adverse Device Effect
AWS	Amazon Web Services
BG	Blood Glucose
BMI	Body Mass Index
CE	Conformite Europeenne
CFR	Code of Federal Regulations
CGM	Continuous Glucose Monitoring
CRA	Clinical Research Associate
CRO	Contract Research Organization
CV	Curricula Vitae
DCCT	Diabetes Control and Complications Trial
DD	Device Deficiency
DIDP	Dawn2 Impact of Diabetes Profile
DKA	Diabetic Ketoacidosis
dL	Deciliter
DQOL	Diabetes Quality of Life
eCRF	Electronic Case Report Form
EC	Ethics Committee
EDC	Electronic Data Capture
EU	European Union
EW	Early Withdrawal
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HCS	Hypoglycemia Confidence Scale
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonization
ID	Identification
IFU	Instructions For Use
INSPIRE	Insulin Dosing Systems: Perceptions, Ideas, Reflections, and Expectations
IOB	Insulin On Board

IRB	Institutional Review Board
ITT	Intention to Treat
MDD	Medical Device Directive
mg	Milligram
mITT	Modified Intention to Treat
mmol	Millimole
MPC	Model Predictive Control
PI	Principal Investigator
PLGS	Predictive Low Glucose Suspend
POC	Point of Care
PP	Per Protocol
PSQI	Pittsburgh Sleep Quality Index
QC	Quality Control
SADE	Serious Adverse Device Effect
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SMP	Safety Management Plan
SUS	System Usability Scale
TIR	Time In Range
T1D	Type 1 Diabetes
T1DDS	Type 1 Diabetes Distress Scale
TSH	Thyroid Stimulating Hormone
TDI	Total Daily Insulin
USADE	Unanticipated Serious Adverse Device Effect
US	United States
UV	Unscheduled Visit

1 INTRODUCTION

Diabetes is a disorder affecting the homeostatic regulation of blood glucose, with potential to cause short-term sequelae of critical hyperglycemia as well as long-term effects of microvascular complications including blindness, kidney disease, and amputation[1] Multiple studies have shown that the risk for long-term complications of diabetes can be reduced by maximizing the time in euglycemia.[2-4] Strict avoidance of hyperglycemia must be balanced with risk for hypoglycemia, a distinctive cause of morbidity and mortality.[5] Furthermore, fear of hypoglycemia is an important barrier to improved glucose control.[6]

The American Diabetes Association (ADA) recommends that adults with type 1 diabetes (T1D) should aim for target A1C levels of less than 7.0% as a goal for glucose control, with the caveat that targets should be individualized and may be higher or lower depending on additional factors.[7] The widespread use of continuous glucose monitoring (CGM) has brought additional granularity to clinical decision-making, and glycemic targets have expanded to include measures like time in range (TIR), defined as percent of CGM readings within the range of 70-180 mg/dL, with TIR of 70% aligning with an A1C of about 7%.[7]

As technology for glucose monitoring has evolved, so has insulin delivery. Connected insulin pumps, including those which suspend insulin delivery during low glucose and with automated insulin delivery algorithms, have become available and improve both TIR and A1C.[8-12]

The Omnipod® 5 Automated Insulin Delivery System (Omnipod 5 System) has a novel algorithm with customizable glucose targets and unique configuration utilizing a tubeless insulin pump (Pod), which is a small (3.9 x 5.2 x 1.45 cm) adhesive patch pump worn on the body. The cannula is automatically deployed directly under the Pod, creating an infusion site without external tubing. The Pod is waterproof (IP28) and is worn continuously for up to 72 hours. All user interactions are conducted wirelessly through a mobile app on a smartphone. The algorithm itself is located on the Pod, and the glucose sensor communicates directly with the Pod through Bluetooth® wireless technology. Therefore, the system can continuously provide automated insulin delivery (AID) via the wearable on-body components alone (Pod and sensor), without the smartphone controller needing to be nearby.

Omnipod 5 was developed through several feasibility studies.[13-16] Subsequently, it was evaluated in a prospective, multi-center, single-arm safety study and shown to be safe and effective in the glycemic management of children, adolescents, and adults ages 2 to 70 years with type 1 diabetes, with minimal episodes of severe hypoglycemia and diabetic ketoacidosis, in addition to significant improvements in glycemic outcomes, including decreased A1C and increased time in range, 70-180 mg/dL.[8,16,17] Among 128 adolescents and adults (14 to 70 years), A1C decreased by 0.38% from 7.16 ± 0.86% at baseline to 6.78 ± 0.68% after 13 weeks of automated mode use. Time in range increased by 9.3% from 64.7 ± 16.6% during a 2-week standard therapy phase where participants used their usual insulin therapy, to 73.9 ± 11.0% with Omnipod 5.[8]

Still, there is little data available allowing a direct comparison of outcomes with the Omnipod 5 system compared to conventional therapy with a CGM and insulin pump without automated features. Data from a study pause during the aforementioned single-arm trial allowed a post-hoc comparison of outcomes with Omnipod 5 with and without the algorithm enabled. During the study, use of the automated insulin delivery function was paused for a mean of 106 days. During the pause, participants could continue study system use without activation of automated delivery where the device functioned as a stand-alone insulin pump (manual mode, 77% of participants), or they could use another insulin regimen (23%). For adolescents and adults who used Omnipod 5 in manual mode during the pause (n=83), TIR was 62.7% during the standard therapy phase, rising to 74.4% during the first automated phase (mean duration 44 days). TIR then decreased to 65.5% with manual mode use during the pause, and then increased again to 73.6% during the second automated phase (mean duration 49 days). This post-hoc crossover comparison provides initial evidence of the additional glycemic benefit achieved by the Omnipod 5 algorithm compared with the same combination of devices used with manual delivery, where the additional benefit from the algorithm is expected to be about 8-12%.[18]

While these results are encouraging, robust comparative efficacy data in a randomized controlled environment is needed for the Omnipod 5 system, as compared to insulin pump with CGM to support changes in standards of care for people with diabetes. As such, this clinical trial aims to determine efficacy and safety of Omnipod 5 in patients with glucose targets above the recommended treatment range.

2 OMNIPOD 5 SYSTEM OVERVIEW

This study will demonstrate the efficacy and safety of the Omnipod 5 System compared to pump and continuous glucose monitor (CGM) therapy in adults with type 1 diabetes currently using pump therapy.

The Omnipod 5 System is developed and manufactured by Insulet Corporation.

The Omnipod 5 Automated Insulin Delivery System used during the study is the system FDA cleared in K203768, K203772, and K203774 and will be used in accordance with its intended use. The Omnipod 5 System was under review for CE mark under the Medical Device Regulation (MDR) in the European Union (EU) at the time of its submission to ANSM/CPP. It has since received CE mark on 16 September 2022 under the reference MDR 744313 R000 (Notified body BSI) and will be used in accordance with its proposed intended use.

3 DEVICE DESCRIPTION OF THE OMNIPOD 5 SYSTEM

The Omnipod 5 System is comprised of two components:

- Omnipod 5 Pod (insulin infusion pump with SmartAdjust technology).
- Omnipod 5 App (installed on the Insulet-provided Controller)

The Dexcom G6 CGM (sold separate and manufactured by Dexcom) is required for use with Omnipod 5 for automated insulin delivery.

The Omnipod 5 Pod interacts with the Omnipod 5 App and a CGM via secure Bluetooth technology. With SmartAdjust technology, the system receives glucose values and trend data from the CGM, automatically calculates insulin dose, and sends delivery commands to the Pod for delivery of insulin. Insulin is delivered through a soft cannula that is automatically inserted by the Pod into the subcutaneous tissue.

The system can work in Automated Mode and Manual Mode. In Automated Mode (SmartAdjust technology activated), the system calculates insulin micro-boluses every five minutes based upon the predicted glucose over a 60-minute prediction horizon. The Omnipod 5 Algorithm adjusts its insulin delivery based on several factors including a user-set glycemic target (110-150 mg/dL) and the user's Total Daily Insulin (TDI). In Manual Mode, the system operates by delivering insulin at programmed basal rates like a standard insulin pump.

The Omnipod 5 App contains a SmartBolus Calculator that is used to deliver meal bolus doses of insulin based on entered carbohydrates as well as sensor and trend data. The SmartBolus Calculator works in both Automated and Manual Modes.

The Omnipod 5 System (with SmartAdjust technology activated) can automatically adjust delivery of insulin based on CGM values and can pause delivery of insulin when the glucose sensor value falls below or is predicted to fall below predefined threshold values. The Omnipod 5 System is currently interoperable with the Dexcom G6 CGM.

Figure 1: System components of the Omnipod 5 System

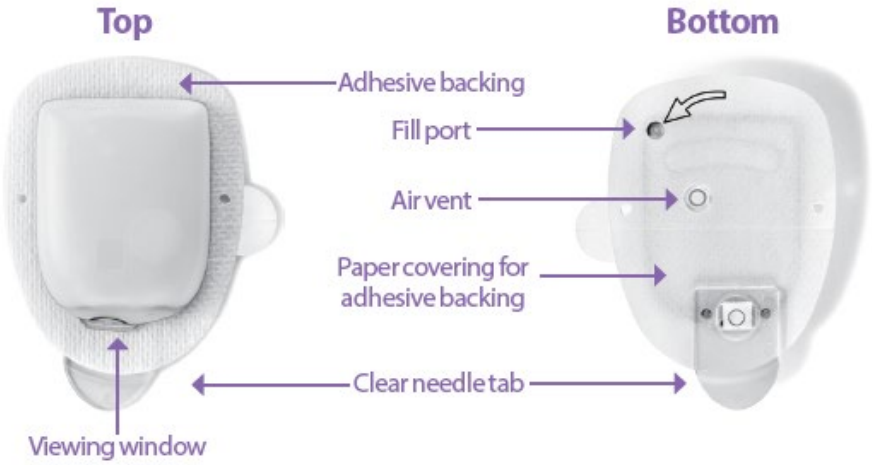

Figure 2:Omnipod 5 Pod

The Omnipod 5 Controller used in this study has an English language user interface. Participants will be provided with the French translated User Guide.

3.1 Indications for Use (EU)

Due to regional regulatory requirements, the indications for use are different for the US and the EU.

The Omnipod 5 System is a single hormone insulin delivery system intended to deliver U-100 insulin subcutaneously for the management of type 1 diabetes in persons aged 6 and older requiring insulin.

The Omnipod 5 System is intended to operate as an automated insulin delivery system when used with compatible CGMs.

When in Automated Mode, the Omnipod 5 System is designed to assist people with type 1 diabetes in achieving glycemic targets set by their healthcare providers. It is intended to modulate (increase, decrease or pause insulin delivery to operate within predefined threshold values using current and predicted CGM values to maintain blood glucose at variable target glucose levels, thereby reducing glucose variability. This reduction in variability is intended to lead to a reduction in the frequency, severity, and duration of both hyperglycemia and hypoglycemia.

The Omnipod 5 System can also operate in a Manual Mode that delivers insulin at set or manually adjusted rates.

The Omnipod 5 System is intended for single patient use. The Omnipod 5 System is indicated for use with Novolog/NovoRapid, Humalog and Admelog U-100 insulin.

3.2 Indication for Use (US)

The Omnipod 5 System in the US consists of 3 regulated devices. The indications for use for the 3 devices are as follows:

The Omnipod 5 ACE Pump (Pod) is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The Omnipod 5 ACE 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 Omnipod 5 ACE Pump is intended for single patient, home use and requires a prescription.

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 6 years of age and older. SmartAdjust technology is intended for single patient use and requires a prescription.

The Omnipod 5 SmartBolus Calculator is software intended for the management of diabetes in persons aged 6 and older requiring rapid-acting U-100 insulin. The Omnipod 5 SmartBolus Calculator calculates a suggested bolus dose based on user-entered carbohydrates, most recent sensor glucose value (or blood glucose reading if using fingerstick), rate of change of the sensor glucose (if applicable), insulin on board (IOB), and programmable correction factor, insulin to carbohydrate ratio, and target glucose value. The Omnipod 5 SmartBolus Calculator is intended for single patient, home use and requires a prescription.

4 DATA PORTAL

Data are securely uploaded from the Omnipod 5 Controller to the Insulet Cloud by both cellular connection and Wi-Fi. Data are then copied from the Insulet Cloud to the Data Portal, which is an application for data analytics and monitoring. The Data Portal currently runs on an Amazon Web Services (AWS) infrastructure. The Data Portal will provide insights including but not limited to time in range, time at each target blood glucose (BG), Automated/Manual Mode comparisons, and time spent in each mode.

Investigators will have access to all uploaded deidentified Omnipod 5 data and be able to view historical trends. The Data Portal will function as the data analytics and monitoring system for this study for those participants randomized to Omnipod 5.

5 STUDY SUMMARY

5.1 Study Purpose

The purpose of this study is to demonstrate the efficacy and safety of the Omnipod 5 System compared to pump and CGM therapy in adults with type 1 diabetes currently using pump therapy.

5.2 Study Design

Adults with type 1 diabetes currently on pump therapy with an A1C between 7-11%, inclusive, will be recruited for the study. At least 80% of participants must have an A1C ≥ 8%. At least 50% of participants must be using Omnipod for pump therapy at the time

of enrollment.

Following a two-week standard therapy period where CGM data will be collected, participants will be randomized in a 2 (Intervention group):1 (Control group) ratio as follows:

- Intervention Group - Omnipod 5 System with Dexcom G6 CGM or
- Control Group – Participant's current insulin pump with Dexcom G6 CGM

Both groups will participate in a randomized period for 13-weeks after completion of standard therapy.

A total of up to 200 participants at up to 15 clinical sites in the US and France will be enrolled in the study, to obtain a minimum of 170 randomized participants.

Table 1:Schedule of Assessments

	Screening	Standard Therapy (14-days)	13 Week Follow Up							
Visit Number	1[a]	2[a]	3	4[h]	5	6	7	8	UV[f]	EW[e]
Study Day/Visit Window	Up to 30-days prior to Study Day 1	14-days prior to Study Day 1	1	2 +1d	14 ±3d	30 ±3d	60 ±3d	90 ±3d	N/A	
Telephone (T) or Office (O) Visit	O	O	O	T/O[d]	T/O[d]	T/O[d]	T/O[d]	O	T/O[d]	O
Screening/Randomization										
Informed Consent	X									
Confirm eligibility	X									
Randomization			X							
Laboratory Assessments										
A1C (Central Lab)	X							X		X
A1C (Point of Care (POC) for eligibility)	X									
TSH, Serum Creatinine, Lipid Panel[b]	X									
Pregnancy Test (urine dipstick)[j]	X		X							
Clinical Assessments										
Medical History	X									
Demographics	X									
Concomitant medications	X	X	X	X	X	X	X	X		X
Height	X									
Weight	X							X		X
Vital signs[c]	X		X	X	X	X	X	X		X
Electrocardiogram	X									
Adverse events		X	X	X	X	X	X	X	X	X
Insulin Delivery (Control arm only after visit 3)[k]			X			X	X	X		X

Questionnaires (See Table 2)										
Study Devices										
Study device training (BG/ketone meter, and CGM)		X								
Dispense/Return QC Tested BG/ketone meter, and CGM		X[h]						X[i]		X[i]
Study CGM sensor placement (Enrollment)		X								
Start/Stop CGM data collection		X						X		X
Assess CGM usage to ensure data criteria has been met[g]		X[g]	X							
Training on Glucagon administration and information on treatment of hypo/hyperglycemia		X								
Omnipod 5 training (Intervention arm only)			X							
Dispense/Return Omnipod 5 System (Intervention arm only)			X					X		X
Data Portal initiation/discontinuation (Intervention arm only)			X					X		X
Complaints/device deficiencies			X	X	X	X	X	X	X	X
BG/ketone meter data review[d]				X	X	X	X	X		X
Pump and CGM data review				X	X	X	X	X	X	X

[a]Screening and Standard Therapy visits may be completed on the same day

[b]TSH, Serum Creatinine and Lipid Panel (includes total cholesterol, HDL, LDL, triglycerides) laboratory assessments within the past 60 days may be used for screening

[c]Vital signs include body temperature, respirations, pulse, and blood pressure should be performed at all in person visits

[d]Visits identified as "T/O" can either be conducted in person at the clinical site or over the telephone. Visits identified as "O" can only be conducted in person at the clinical site. Vital signs are not required at any visit conducted via telephone, however, BG/Ketone meter data review should still occur

[e]Early withdrawal visit will only be conducted for participants who complete visit 3 and discontinue prior to visit 8

[f] Unscheduled visits will serve as extra study visits, if needed

[g] Participants meeting the CGM usage and data criteria with their own Dexcom G6 will be eligible to immediately commence the study at Visit 3 (in which case, visit 1, visit 2, and visit 3 may occur on the same day). CGM data for EU subjects during Standard Therapy will be collected prospectively, and thus EU Subjects will need to participate in the full 14-day Standard Therapy phase.

[h] BG/ketone meter must pass at least one level of quality control testing prior to dispensing

[i] Undispensed BG/ketone meters do not need to be returned to sponsor

[j] Pregnancy tests are only required at both visit 1 and visit 3 if these visits do not occur on the same day

[k] Insulin delivery data will be collected and documented on a case report form for the control arm, the intervention arm data will automatically be collected by Insulet cloud

Abbreviations: S=Screening; EW=Early Withdrawal; QC=Quality Control Testing; UV=Unscheduled Visit

Table 2:Patient Reported Outcomes (Questionnaires)

Visit	Adult (ages 18-70)
Visit 2 Standard Therapy	Clarke EQ-5D-3L T1DDS DQOL-brief DIDP HCS PSQI SUS INSPIRE-Adult
Visit 8 (End of Study) or Early Withdrawal	Clarke EQ-5D-3L T1DDS DQOL-brief DIDP HCS PSQI SUS INSPIRE-Adult

6 OBJECTIVES AND ENDPOINTS

6.1 Primary Objective

To demonstrate superior efficacy of the Omnipod 5 System compared to pump and CGM therapy in adults with type 1 diabetes.

6.1.1 Primary Endpoint

The primary endpoint is per-participant percentage of time in range (TIR) 70-180 mg/dL as measured by study CGM and comparing the Intervention group to the Control group during the 13 week randomized period.

6.2 Secondary Objective

To demonstrate additional measures of efficacy and safety of the Omnipod 5 System compared to pump and CGM therapy in adults with type 1 diabetes.

6.2.1 Secondary Endpoints

The following secondary per-participant endpoints will be evaluated and compared in the Intervention group vs. Control group at the end of the 13-weekrandomized period:

- Percentage of time <54 mg/dL (non-inferiority)
- Percentage of time >180 mg/dL
- Mean glucose
- Change from baseline in A1C
- Percentage of time < 70 mg/dL
- Change from baseline in T1-DDS total score
- Change from baseline in HCS total score
- Change from baseline in DQOL-brief total score

6.3 Exploratory Endpoints

The following exploratory endpoints will be evaluated and compared in the Intervention group vs. Control group at the end of the 13-week randomized period:

- Proportion of participants with A1C <7%
- Proportion of participants with A1C <8%
- Proportion of participants with ≥1% improvement in A1C from baseline
- Proportion of participants with ≥10 relative percentage point improvement in A1C from baseline
- Proportion of participants with either ≥1% improvement in A1C from baseline OR ≥10 relative percentage point improvement in A1C from baseline
- Change from baseline in Body Mass Index (BMI)
- Change from baseline in total daily insulin (TDI) (units/kg)
- Additional CGM-derived endpoints, such as coefficient of variation, time above range >250 mg/dL, percentage of time < 54 mg/dL (superiority), TIR during daytime and nighttime hours
- Number of episodes of severe hypoglycemia
- Number of episodes of DKA

6.4 Patient Reported Outcomes

Questionnaires will be used to evaluate general and disease-specific quality of life, and device usability. Results will be assessed at 13 weeks compared to baseline (Intervention and Control group)

- Clarke Hypoglycemia Awareness
- EQ-5D-3L – Used to measure quality of life
- T1-DDS[1] – Used to measure four critical dimensions of distress
- DQOL-brief[2] – Used to assess the relative burden of an intensive diabetes treatment regimen
- DIDP – Used to assess the perceived impact of diabetes in physical health, finances, relationships with family/friends, leisure activities, work/studies and emotional well-being
- HCS[3] – Used to measure hypoglycemia unawareness, hypoglycemia frequency, severity, and impact
- PSQI – Used to measure sleep disturbance and usual sleep habits
- SUS – Used to measure usability of a system
- INSPIRE – Used to evaluate the impact of AID systems on the psychosocial functioning and quality of life

7 SCREENING AND ELIGIBILITY

A total of up to 200 participants aged 18-70 years with type 1 diabetes currently on pump therapy with an A1C between 7-11%, inclusive, will be recruited for the study. A screening visit will be scheduled for the potential participant for the clinical site to assess eligibility. Participants who appear to meet the eligibility criteria will review and sign an informed consent form (ICF). Once the informed consent form has been signed and eligibility assessments have been completed and confirmed, study participants will be eligible to enroll in the study. Enrollment will occur when the participant begins wearing the Dexcom G6 CGM dispensed for the study. All study participants will receive Dexcom G6 CGM device training prior to enrollment. Commencement of the standard therapy period will follow placement of the Dexcom G6 CGM.

Participants who do not meet the eligibility criteria will not continue in the study and will be considered screen failures.

Laboratory results within the last 60 days, except for A1C, may also be used if available.

At the conclusion of the standard therapy period, participants will be randomized and assigned to either the Intervention group or the Control group using 2:1 randomization. Twice as many participants are expected to be randomized to the Intervention group versus the Control group.

After completing the 14-day standard therapy period, participants randomized to the Intervention arm will be trained on the Omnipod 5 system, and all participants will transition to the 13-week period of the study. Participants randomized to the control arm

[1] Change from baseline in T1-DDS total score at 13 weeks is a secondary endpoint.
[2] Change from baseline in DQOL-brief total score at 13 weeks
[3] Change from baseline in HCS total score at 13 weeks is a secondary endpoint.

will continue their usual pump therapy for the 13-week period of the study while using the study CGM.

7.1 Visit 1 (Up to 30 days prior to Study Day 1)

Visit 1 will be conducted in person at the clinical study site. This visit will assess eligibility and will include:

- Signing of informed consent
- Review of inclusion/exclusion criteria and confirmation of eligibility
- Assessments performed following Table 1:Schedule of Assessments

7.1.1 Informed Consent

Participants who appear to meet the eligibility criteria will be asked to review and sign an ICF approved by each respective Institutional Review Board (IRB) or Ethics Committee (EC) for participation in the study before any procedure or collection of any data that are not part of usual care.

Participants will be required to sign a statement of informed consent that meets the requirements of 21 CFR part 50, local regulations, ICH guidelines, Health Insurance Portability and Accountability Act (HIPAA) requirements, where applicable, and the IRB/IEC or study center.

After informed consent is obtained, a participant identification number will be issued to uniquely identify each participant. The unique identifier will be used to identify the participant throughout the study and will be used for all source documents and electronic Case Report Forms (eCRFs).

7.1.2 Confirm Eligibility

7.1.2.1 Inclusion Criteria

Participants must meet all the following criteria to be enrolled in the study:

1. Age at time of consent 18-70 years of age
2. Diagnosed with type 1 diabetes for at least 1 year. Diagnosis is based on investigator's clinical judgment.
3. On pump therapy for at least ≥ 3 months prior to screening and familiar with pump therapy concepts such as basal and bolus insulin delivery, and carbohydrate counting. Participants using automated insulin delivery (AID) devices, including devices with predictive low glucose suspend (PLGS), in the 3 months prior to screening, will be excluded from participating.
4. A1C 7.0-11.0% by point-of-care taken at screening visit
5. Willing to use and obtain U-100 insulin: (either insulin aspart (Novolog, NovoRapid), or insulin lispro (Humalog, Admelog)), as the primary insulin treatment
6. Must have a smartphone that supports the Dexcom app download and participants must be willing to use the app throughout the study
7. Investigator has confidence that the participant can safely operate all study devices and can adhere to the protocol
8. Willing to wear the system continuously throughout the study
9. Willing and able to sign the Informed Consent Form (ICF)

7.1.2.2 Exclusion Criteria

Participants who meet any of the following criteria will be excluded from the study:

1. Any medical condition, such as untreated malignancy, unstable cardiac disease, unstable or end-stage renal failure, eating disorders, or other conditions which in the opinion of the investigator, would put the participant at an unacceptable safety risk
2. History of severe hypoglycemia in the past 6 months
3. History of diabetic ketoacidosis (DKA) in the past 6 months, unrelated to an intercurrent illness or infusion set failure
4. Blood disorder or dyscrasia within 3 months prior to screening, including use of hydroxyurea, which in the investigator's opinion could interfere with determination of HbA1C
5. Currently on systemic steroids or intends to receive systemic steroid treatment in the next 6 months, including stable treatment for adrenal insufficiency. Inhaled, ophthalmic, topical, joint injection, and other locally applied steroids are allowed.
6. Unable to tolerate adhesive tape or has any unresolved skin condition in the area of sensor or pump placement
7. Use of non-insulin anti-hyperglycemic medication other than metformin, in the 12 weeks prior to the Baseline Visit. Participants taking metformin should remain on a steady dose during study participation.
8. Pregnant or lactating, or is a woman of childbearing potential and not on acceptable form of birth control (acceptable forms of contraception include abstinence, barrier methods such as condoms, hormonal contraceptives, intrauterine device, surgical sterilization such as tubal ligation or hysterectomy, or vasectomized partner)
9. Participation in another clinical study using an investigational drug or device within 30-days or 5 half-lives (whichever is longer) prior to screening, or intends to participate in any other study during this study period
10. Unable to follow clinical protocol for the duration of the study or is otherwise deemed unacceptable to participate in the study per the investigator's clinical judgment
11. Participant is an employee of Insulet, an Investigator or Investigator's study team, or immediate family member of any of the aforementioned

7.1.3 Lab and Clinical Screening Assessments

Participants who have signed the informed consent and appear to meet the eligibility criteria will continue to the screening assessments which will be performed at the clinical study site.

Assessments may be completed up to 30-days prior to enrollment. Participants are considered enrolled upon placement of the first study CGM. Assessments include the following:

- A1C (Central Lab)
- A1C (Point of Care for eligibility)

- TSH, Serum Creatinine, Lipid Panel (includes total cholesterol, HDL, LDL, triglycerides, assessments within the past 60 days may be used for screening)
- Pregnancy test (urine dipstick) for women of childbearing potential
- Medical history (including prior and current medical conditions and surgical history)
- Demographics (age, gender, race (US only), ethnicity (US only))
- Review of concomitant medications
- Height & weight
- Vital signs (body temperature, respirations, pulse, and blood pressure)
- Electrocardiogram

Clinical sites will send a blood specimen for A1C to a central laboratory. A point of care (POC) A1C will be used to determine eligibility.

7.2 Visit 2 (14-days prior to Study Day 1)

Visit 2 will be conducted in person at the clinical study site and may be combined with Visit 1 if all eligibility criteria are met and laboratory assessments are determined to meet study criteria. All scheduled assessments will be performed according to Table 1:Schedule of Assessments and Table 2:Patient Reported Outcomes (Questionnaires).This visit will include:

- Review of concomitant medications
- Assessment of AEs
- Questionnaires (Table 2:Patient Reported Outcomes (Questionnaires))
- Study device training per manufacturer's instructions (CGM and BG/ketone meter)
- Dispense BG/ketone meter, and CGM:
  - BG/ketone meter
  - Contour® Next One blood glucose meter (US sites only)
  - Contour® Next One blood glucose meter test strips (US sites only)
  - Precision Xtra blood ketone meter (US sites only)
  - Precision Xtra blood ketone meter test strips (US sites only)
  - FreeStyle Optium Neo blood glucose and ketone meter (EU sites only)
  - FreeStyle Optium Neo blood glucose and ketone strips (EU sites only)
  - Lancets
  - Dexcom G6 CGM (sensor and transmitter)
  - CGM Data Collection Device (EU sites only)
- QC testing of BG/ketone meter
  - Must pass at least one level of quality control testing prior to dispensing
- Study CGM sensor placement (Enrollment)
  - Assess CGM usage and data criteria are met for participants currently using Dexcom G6 (US sites only).
  - Sensor placement location will be reinforced as well as the importance of using approved locations
  - Ensure all participants understand how to troubleshoot sensor errors and avoid over-calibration of sensors
- Start CGM data collection

- Training on glucagon administration and information on treatment of hypo/hyperglycemia

7.2.1 Assessment of CGM Usage and Data Criteria

7.2.1.1 Current Dexcom G6 Users (US Sites Only)

Current Dexcom G6 users may be exempt from the standard therapy 14-day period if the following criteria are met:

- Willing to provide 14-days of CGM data from the past 30-days
- Meet the success criteria of 80% CGM use during any consecutive 14-days in the past 30-days
- Must have ≥ 2,016 CGM values during the 14-days

The site staff will review the device use and data criteria to see if they have met the exemption criteria. If exemption criteria are not met, participants may choose to continue to collect data until they meet the criteria or will be required to participate in the entire 14-day standard therapy period consistent with the requirements for non-G6 users.

If participants meet the criteria, they will be immediately eligible to proceed with Visit 3, in which case Visit 1, Visit 2, and Visit 3 may occur on the same day, commencing the 13-week study.

7.2.1.2 Non-G6 Users (US Sites Only)

All non-G6 users will be required to participate in the entire standard therapy 14-day period. At the commencement of standard therapy, participants will be dispensed an unblinded Dexcom G6 CGM and will be instructed on how to download the Dexcom app on their personal cellular devices. The site staff will link the participant's Dexcom app with the data collection portal. Participants will commence the 14-day period data collection period.

7.2.1.3 CGM Data Criteria (EU Sites Only)

All subjects in the EU will be required to participate in the entire standard therapy 14-day period. At the commencement of standard therapy, participants will be dispensed a Dexcom G6 CGM and a CGM data collection device. The site staff will link the CGM data collection device with the data portal. Participants will commence the 14-day data collection period.

7.3 CGM Usage

During the standard therapy 14-day period, participants will be asked to do the following:

- Manage their diabetes at home per their usual routine
- Administer meal boluses per their usual dosing routine
- Change their sensor if a sensor fails, or as needed
- Calibrate their CGM, if required, per the manufacturer's instructions
- Monitor their capillary blood glucose (BG) as needed

At the conclusion of the 14-day standard therapy period, the data criteria will be reviewed to see if they have met the device use and data criteria. If criteria are not met, participants may choose to continue to collect data until they meet the criteria. Extending standard therapy past 14-days will not constitute a protocol deviation unless standard therapy extends past 30-days. If participants extend beyond the 14-days, the most recent 14-days of data meeting the criteria defined for CGM use and data criteria will be used in the endpoint analysis.

7.3.1 CGM Initiation

Participants will be provided with the Dexcom G6 CGM and instructed to use the devices throughout the study. Dexcom G6 CGM training will be provided to all participants. Current CGM users will be instructed to remove their personal CGM and place the study Dexcom G6 CGM. Participants will be instructed to only use the study provided Dexcom G6 CGM device for the duration of the study.

Participants will be provided with contact information for the clinical study site and advised to contact the site for any health or device related issues.

7.4 Visit 3 (Study Day 1)

Visit 3 will mark the start of the 13-week study and will commence upon the conclusion of the standard therapy 14-day period and after all assessments are performed according to Table 1:Schedule of Assessments

Visit 3 will be conducted in person at the clinical study site. All scheduled assessments will be performed according to Table 1:Schedule of Assessments This visit will include:

- Randomization
- Pregnancy test (urine dipstick) for women of childbearing potential (required only if Visit 1 and Visit 3 do not occur on the same day)
- Review of concomitant medications
- Vital signs
- Assessment of AEs
- Insulin delivery metrics (e.g., TDI, average basal and bolus insulin dose, and time on device over the past 30 days)
- Assess CGM usage and data criteria has been met (at least 80% CGM use (11.2-days) during any consecutive 14-days in the past 30-days and ≥ 2,016 CGM values during the 14-days)
- All participants are required to have access to glucagon and receive training on how to deliver the medication
- Omnipod 5 System device training conducted by trained clinical site staff (Intervention arm only)
- Dispense Omnipod 5 System (Intervention group only)
- Data Portal initiation (Intervention group only)
- Dispense Dexcom CGM and confirm data transmission for those in control arm (Control group only)
- Complaints/device deficiencies since last visit

7.4.1 Randomization

Participants who meet all eligibility criteria, have completed all screening assessments, and have met the CGM device usage and data criteria will be randomized 2:1 using a computer-generated randomization scheme stratified by site, A1C (7% to <8% vs. ≥8% to 11%), and Omnipod use (user vs. non-user). A permuted-block randomization scheme will be implemented to balance group assignments. Randomization will be assigned via study database access during Visit 3 to the two study groups (Intervention Group: Omnipod 5 System with Dexcom G6 CGM or Control Group: Participant's current pump with Dexcom G6 CGM).

During the 13-week study period, all participants will be asked to do the following:

- Follow insulin therapy per recommendations from the clinical study staff
- Follow their pre-exercise management such as insulin reduction for meal boluses, consumption of snacks, or adjusting their insulin delivery settings
- Treat themselves per their usual routine if they become hypoglycemic or hyperglycemic or have symptoms of either at any time during the study
- Consume meals and snacks of their own choosing. Participants will be encouraged to estimate the grams of carbohydrates for each meal or snack per their usual routine. The estimate should be entered into the meal bolus calculator.
- Give meal boluses per their usual dosing routine
- Change their CGM per manufacturer's instructions or sooner if necessary
- Change the Pod at least once every 72 hours (Intervention group only)
- Change pump infusion site as recommended by manufacturer

In the event of unexplained hyperglycemia, where the CGM is >300mg/dL for 1 hour or >250 mg/dL for 2 hours, blood glucose (measured with BG meter) and ketones should be checked. If BG is ≥300 mg/dL and ketones are >1.0 mmol/L, an occlusion or dislodged cannula should be suspected. The Pod or infusion set should be removed, and the participant will be instructed to replace the Pod or infusion set at a different location on the body. Participants should contact the clinical site for further instructions to determine whether an additional injection of insulin is required. This prolonged hyperglycemic event, defined as meter BG ≥300 mg/dL and ketones >1.0 mmol/L, will be recorded as an adverse event.

7.5 Visits 4 and 5

Visit 4 and 5 will be conducted either over the telephone or in person at the clinical study site on study days 2 (+1d) and 14 (±3d) respectively. All scheduled assessments will be performed according to Table 1:Schedule of Assessments These visits will include:

- Review of concomitant medications
- Vital signs (for in person visits)
- Assessment of AEs
- Complaints/device deficiencies since last visit
- BG/ketone meter data review by clinician

- Pump and CGM data review by clinician

7.6 Visits 6 and 7

Visit 6 and 7 will be conducted either over the telephone or in person at the clinical study site on study day 30 (±3d) and 60 (±3d). All scheduled assessments will be performed according to Table 1:Schedule of Assessments This visit will include:

- Review of concomitant medications
- Vital signs (for in person visits)
- Assessment of AEs
- Complaints/device deficiencies since last visit
- BG/ketone meter data review by clinician
- Insulin delivery metrics (e.g., TDI, average basal and bolus insulin dose, and time on device over the past 30 days) (Control group only)
- Pump and CGM data review by clinician

7.7 Visit 8

Visit 8 will be conducted in person at the clinical study site on study day 90(±3d). All scheduled assessments will be performed according to Table 1:Schedule of Assessments This visit will include:

- A1C (central laboratory)
- Review of concomitant medications
- Weight
- Vital signs
- Assessment of AEs
- Insulin delivery metrics (e.g., TDI, average basal and bolus insulin dose, and time on device over the past 30 days) (Control group only)
- Completion of questionnaires (Table 2:Patient Reported Outcomes (Questionnaires))
- Return BG meter, Ketone meter, and study CGM, if unused
- Stop CGM data collection
- Return Omnipod 5 System (Intervention group only)
- Data Portal (Intervention group only) discontinuation
- Complaints/device deficiencies since last visit
- BG/ketone meter data review by clinician
- Pump and CGM Data review by clinician

7.8 Unscheduled Visits

Aside from scheduled visits, participants may require an unscheduled visit either by telephone or in person at the clinical study site. All assessments will be performed according to Table 1:Schedule of Assessments . This visit will include, at a minimum:

- Assessment of AEs
- Complaints/device deficiencies since last visit
- Pump and CGM data review by clinician

Additional assessments, including review of BG/ketone meter data, may be warranted at the discretion of the investigator.

Unscheduled visits should be documented when there is meaningful contact with the subject, such as when updating device settings, subject retraining, or any in-person contact. Basic or minor contacts to discuss subject visit scheduling, device questions, subject reminders, requests for or providing additional supplies, or follow up activities related to another scheduled visit should not be documented as an Unscheduled Visit.

Instructions will be given to participants on how to contact clinical study staff 24 hours per day to report any study related problems. Participants will be encouraged to call the clinical study site at any time with any concerns.

7.9 Early Withdrawal

Any participant may withdraw from the study at any time for any reason. Upon withdrawal, assessments will be performed following Table 1:Schedule of Assessments and Table 2:Patient Reported Outcomes (Questionnaires). The investigator may also terminate a participant's participation in the study if it is in the best interest of the participant or if the Sponsor or local regulatory agency terminates the study.

The Early Withdrawal visit will include:

- A1C (central laboratory)
- Review of concomitant medications
- Weight
- Vital signs
- Assessment of AEs
- Insulin delivery metrics (e.g., TDI, average basal and bolus insulin dose, and time on device) (Control group only)
- Completion of questionnaires (Table 2:Patient Reported Outcomes (Questionnaires)
- Return BG meter, Ketone meter, and study CGM, if unused
- Return Omnipod 5 System (Intervention group only)
- Stop CGM data collection
- Data Portal discontinuation (Intervention group only)
- Complaints/device deficiencies such as occlusion alarms and system hazard alarms since last visit
- BG/ketone meter data review by clinician
- Pump and CGM data review by clinician

The reason for withdrawal will be recorded, and their participation in the study will end.

In the event of a participant's death during the study, the participant's participation will be considered terminated, and the date of death will be used as the date of study exit.

7.10 Lost to Follow-up

Every effort will be made to contact a participant in the event of a missed scheduled visit. A participant will be considered lost to follow-up if they are inaccessible by two or more

different methods of contact and fail to show up for two scheduled visits. The site will document each attempt made to contact the participant and specify the reason for early withdrawal as lost to follow-up.

8 SPONSOR REPRESENTATIVES

One or more representatives of the Sponsor may be present at the clinical study site during study visits under supervision of study site personnel.

9 SAFETY

9.1 Types of Known Risks and Benefits

There are known risks and benefits. Most of the risks are not unique to the study and are typical for patients using insulin pumps, CGM, and BG meters. For the Control group, the applicable Instructions for use (IFU) should be referenced for any additional potential risks.

The known risks are as follows:

- Hypoglycemia and/or hyperglycemia as a result of change in diet, activity, diabetes management or insulin regimen during the study.
- Hypoglycemia and/or hyperglycemia as a result of over or under delivery of insulin due to a device defect, failure or malfunction of any of the system components.
- Hypoglycemia, hyperglycemia, diabetic ketoacidosis, seizure, coma or death related to insulin administration, pump use or misuse, or Omnipod 5 System use or misuse.
- Use of the Pod – because the Pod uses only rapid-acting insulin, users are at increased risk for developing hyperglycemia if insulin delivery is interrupted. If it is untreated, prolonged hyperglycemia can lead to diabetic ketoacidosis (DKA). DKA can cause symptoms such as breathing difficulties, shock, coma, or death. Further, occlusions can interrupt insulin delivery and lead to hyperglycemia or DKA. Other potential risks associated with using the Pod are:
  - Anaphylaxis (allergic shock)
  - Bruising at the Pod site
  - Bleeding at the Pod site
  - Erythema (redness at the Pod site)
  - Excoriation (raw skin at Pod site)
  - Pruritus (itching)
  - Induration (hardening of the skin at the Pod site)
  - Infection (can include heat, redness, swelling, pain, and drainage)
  - Inflammation (redness, swelling)
  - Skin reaction to adhesive at the Pod site
  - Papule (small, solid raised area on the skin similar to a pimple)
  - Pain or discomfort
  - Ulceration (skin sores)
  - Vesicles (blisters)
- Use of the CGM – risk of bruising, infection, pain and/or bleeding at the site of insertion, and skin site reaction to adhesive

- Use of the Controller – risk of overheating of the Omnipod 5 Controller charging port and cable, including the cable melting, deforming, or discoloring. The excess heat may cause minor burns if those areas of the controller are touched or could lead to fire.
- On rare occasions, the CGM sensor may break and leave a small portion of the sensor under the skin that may cause redness, swelling, or pain at the insertion site, and may require surgical removal.
- Blood sampling with fingerstick – minor discomfort and risk of infection at site of fingerstick

There may be no direct benefits to participating in this study however knowledge will be gained that may benefit others. In addition, participants may experience improvements in glycemic control.

9.2 Hypoglycemia/Hyperglycemia

Participants will be asked to treat per their usual routine if they suspect either hypoglycemia or hyperglycemia, either by confirmation of hypoglycemia with a fingerstick BG, symptoms, or perceived risk.

Participants will be encouraged to manage their hyperglycemia per their usual routine. This includes checking for ketones and administering a correction bolus if needed.

In the event of unexplained hyperglycemia, where the CGM is >300mg/dL for 1 hour or >250 mg/dL for 2 hours, blood glucose (measured with BG meter) and ketones should be checked. If BG is ≥300 mg/dL and ketones are >1.0 mmol/L, an occlusion or dislodged cannula should be suspected. The Pod or infusion set should be removed, and the participant will be instructed to replace the Pod or infusion set at a different location on the body. Participants should contact the clinical site for further instructions to determine whether an additional injection of insulin is required. This prolonged hyperglycemic event, defined as meter BG ≥300 mg/dL and ketones >1.0 mmol/L, will be recorded as an adverse event.

9.3 Adverse Events

Adverse Event (AE): is defined as any untoward medical occurrence, unintended disease or injury, or any untoward clinical signs (including an abnormal laboratory finding) in participants, users or other persons, whether or not related to the investigational medical device.

NOTE 1: This includes events related to the investigational medical device or the comparator.[22]

NOTE 2: This definition includes events related to the procedures involved (any procedure in the clinical investigation plan).[22]

Serious Adverse Event (SAE): Any untoward medical occurrence that:

- Led to death
- Led to serious deterioration in the health of the participant, that either resulted in:

- a life-threatening illness or injury, or
- a permanent impairment of a body structure or a body function, or
- hospitalization, or prolonged existing hospitalization, or
- medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.

- Led to fetal distress, fetal death, or a congenital abnormality or birth defect.

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered a serious adverse event.[22]

Unanticipated Serious Adverse Device Effect (USADE): Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of participants. [22]

Adverse Device Effect (ADE): An adverse device effect (ADE) is an adverse event related to the use of an investigational medical device.[22]

NOTE 1: This definition includes any adverse event resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device. [22]

NOTE 2: This definition includes any event resulting from user error or from intentional misuse of the investigational medical device. [22]

An event that occurs solely due to participant (i.e., user) error in which the device functions properly generally will not be considered an ADE unless it is determined that the instructions on the screen of the device or user manual (or similar training materials) may have contributed to the event (note: the event may still meet criteria for reporting as an adverse event).

Serious Adverse Device Effect (SADE): A serious adverse device effect is defined as an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event. [22]

Anticipated Serious Adverse Device Effect (ASADE): anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.

Device Deficiency (DD): A device deficiency is defined as a device related complaint or malfunction or any inadequacy of a device with respect to its identity, quality, durability, reliability, safety or performance and includes misuse or use errors and inadequate labeling. A device deficiency is something that happens to a device or is related to device performance, whereas an adverse event happens to a participant. A device deficiency may occur independently from an AE, or along with an AE. An AE may occur without a device deficiency or there may be an AE related to a device deficiency.

For any event where there is suspicion that the Omnipod 5 study device is involved, the Sponsor will request that the investigator return the device component for evaluation.

All device deficiencies will be reported to the Sponsor within 3 business days of knowledge of the deficiency and documented on an appropriate eCRF. Once entered, notifications will be sent automatically to Sponsor. Alternate reporting methods will be provided to site for notifying Sponsor if database entry is inaccessible. All device components associated with a reported device deficiency (Controller, Pod, and CGM) should be retained at the clinical site and returned to the Sponsor or CGM manufacturer for investigation and analysis.

9.4 Reportable Adverse Events

Adverse events will be assessed on an ongoing basis throughout the study. Adverse event reporting will begin at the start time of the standard therapy (i.e., insertion of the CGM sensor) and continue until the participant's participation has ended. All adverse events must be followed until resolution, or until the AE has stabilized, or until the study has been completed.

Pre-existing medical conditions or symptoms observed prior to the start time of the standard therapy phase will not be recorded as an AE and should be collected in the participant's medical history. In the event there is a change (i.e., worsening) in the pre-existing medical condition or symptoms after enrollment meeting the criteria of a reportable adverse event, then an AE must be reported.

For this protocol, a reportable adverse event includes any untoward medical occurrence that meets one of the following criteria:

1. An SAE
2. An ADE unless excluded from reporting in Hypoglycemic Events and Hyperglycemic/Ketotic Events sections below
3. An AE not related to a study device issue which leads to temporary or permanent discontinuation of the study devices or the participant's own insulin pump, or creates a clinically significant impact on a participant's glucose control
4. An AE that affects the participant's ability to complete any study procedures
5. An AE for which a visit is made to a hospital emergency department
6. Hypoglycemic Events as defined below
7. Hyperglycemia/Ketotic Events as defined

9.5 Hypoglycemic Events

Hypoglycemia is only reportable as an adverse event when one of the following criteria is met:

- Severe Hypoglycemia: The event required assistance of another person due to altered consciousness, and required another person to actively administer carbohydrate, glucagon, or other resuscitative actions[21]. This means that the participant was impaired cognitively to the point that he/she was unable to treat himself/herself, was unable to verbalize his/her needs, was incoherent, disoriented, and/or combative, or experienced seizure or loss of consciousness. These episodes may be associated with sufficient neuroglycopenia to induce seizure or loss of consciousness. If plasma

glucose measurements are not available during such an event, neurological recovery attributable to the restoration of plasma glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose concentration.
- Hypoglycemia resulting in an SAE that may not otherwise meet the definition of Severe Hypoglycemia defined above.

When a hypoglycemic event meets the above reporting requirements, an Adverse Event Form should be completed. A severe hypoglycemia event should be considered a serious adverse event and follow the SAE reporting requirements.

9.6 Hyperglycemic/Ketotic Events

Hyperglycemia is only reportable as an adverse event when any of the following criteria is met:

- The event involved DKA, as defined by the Diabetes Control and Complications Trial (DCCT)[20] , i.e. if all of the following are present:
  - Symptoms such as polyuria, polydipsia, nausea, or vomiting;
  - Serum ketones >1.5 mmol/L or large/moderate urine ketones;
  - Either arterial blood pH <7.30 or venous pH <7.24 or serum bicarbonate <15; and
  - Treatment provided in a health care facility
- Evaluation or treatment was obtained at a health care provider facility for an acute event involving hyperglycemia or ketosis, or the participant contacted the site and received guidance on how to manage the hyperglycemia/ketosis
- Prolonged hyperglycemia: defined as meter BG ≥300 mg/dL for over 1 hour and ketones >1.0 mmol/L
- Hyperglycemia resulting in an SAE that may not otherwise meet the above criteria

When a hyperglycemia/ketotic event meets the above reporting requirements, Adverse Event Form should be completed.

Events meeting DKA criteria should be considered a serious adverse event and follow the SAE reporting requirements. Hyperglycemia events not meeting criteria for DKA generally will not be considered as serious adverse events unless one of the SAE criteria above is met

9.7 Relationship of Adverse Event to Devices or Study Procedures

The investigator will be responsible for deciding on the causal relationship of the AE. Specifically, the investigator will report whether the AE was related to study procedures and/or related to the devices (participant's own insulin pump, study CGM and Omnipod 5).

To ensure consistency of adverse event causality assessments, investigators should apply the following general guidelines when determining whether an adverse event is related.

The causal relationship to the study procedures and the devices for each adverse event will be rated as follows:

- Unrelated: The event is not related to the procedures or the investigational device.
- Possibly Related: The temporal sequence is such that the relationship is not unlikely or there is no contradicting evidence that can reasonably explain the participant's condition. There is a possibility of any relation between the event and the procedures or the devices.
- Related: The temporal sequence is relevant, or the event abates upon completion of the procedure/ use of devices, or the event cannot be reasonably explained by the participant's condition or comorbidities. The event is related or most likely associated with the procedures or the devices.

9.8 Severity (Intensity) of Adverse Events

The severity (intensity) of an adverse event will be rated on a three-point scale: (1) mild, (2) moderate, or (3) severe. A severity assessment is a clinical determination of the intensity of an event. Thus, a severe adverse event is not necessarily serious. For example, itching for several days may be rated as severe, but may not be clinically serious.

- Mild: Usually transient, requires no special treatment, and does not interfere with the participant's daily activities.
- Moderate: Usually causes a low level of inconvenience, discomfort or concern to the participant and may interfere with daily activities but is usually ameliorated by simple therapeutic measures and participant is able to continue in study.
- Severe: Interrupts a participant's usual daily activities, causes severe discomfort, may cause discontinuation of study device, and generally requires systemic drug therapy or other treatment.

9.9 Outcome of Adverse Events

The outcome of each reportable adverse event will be classified by the investigator as follows:

- Recovered/Resolved – The participant recovered from the AE/SAE without sequelae. Record the AE/SAE stop date.
- Recovered/Resolved with Sequelae – The event persisted and had stabilized without further anticipated change in the event status. Record the AE/SAE stop date.
- Fatal – A fatal outcome is defined as the SAE that resulted in death. Only the event that was the cause of death should be reported as fatal. AEs/SAEs that were ongoing at the time of death; however, were not the cause of death, will be recorded as "resolved" at the time of death.
- Not Recovered/Not Resolved (Ongoing) – An ongoing AE/SAE is defined as the event was ongoing with an undetermined outcome.
    - An ongoing outcome will require follow-up by the site in order to determine the final outcome of the AE/SAE or until participant completes the study.
    - The outcome of an ongoing event at the time of death that was not the cause of death, will be updated and recorded as "resolved" with the date of death recorded as the stop date.

- Unknown – An unknown outcome is defined as an inability to access the participant or the participant's records to determine the outcome (for example, a participant that was lost to follow-up).

If any USADEs are ongoing when a participant completes the study (or withdraws), the participant will continue to be followed until the event resolves or has no prospect of improvement or change, even after the participant has completed all applicable study visits/contacts, unless that participant has withdrawn their consent. For all other reportable adverse events, data collection will end at the time the participant completes the study. Note: Participants should continue to receive appropriate medical care for an adverse event after their participation in the study ends.

9.10 Reportable Device Issues

Device deficiencies will be reported except in the following circumstances. These occurrences are expected and will not be reported on a Device Deficiency Form:

- CGM sensor, Pod or infusion set lasting fewer days than expected per manufacturer
- CGM tape, Pod or infusion set adherence issues
- Battery lifespan deficiency of the Controller due to inadequate charging or extensive wireless communication
- Intermittent device communication issues not requiring replacement
- Device issues, including alerts and alarms, clearly addressed in the user guide that do not require additional troubleshooting

9.11 Timing of Event Reporting

SAEs possibly related or related to a study device or study procedures and UADEs must be reported to the Sponsor/CRO within 2 business days of the site becoming aware of the event. This can occur via phone or email to the CRA/site monitor or Study Physician, or by completion of the AE eCRF. If the form is not initially completed, it should be completed as soon as possible after there is sufficient information to evaluate the event. All other reportable AEs should be submitted by completion of the AE eCRF within 5 business days of the site becoming aware of the event.

Each principal investigator is responsible for reporting adverse events required by this protocol and abiding by any other reporting requirements specific to his/her Institutional Review Board or Ethics Committee.

Upon receipt of a USADE report, the Sponsor will investigate the UADE and if indicated, report the results of the investigation to all participating investigators, overseeing IRBs or ECs, and Regulatory Authorities within 7 calendar days of the Sponsor becoming aware of the USADE. Copies of the associated reports and correspondence with the investigators, regulatory authorities, and Sponsor must be retained with study records.

The Medical Monitor will determine if the USADE presents an unreasonable risk to participants as described in the safety management plan (SMP) and in accordance with local regulations.

Device deficiencies will be handled by the Sponsor or designee.

If the participant is hospitalized because of or during the course of an SAE, then a copy of the hospital discharge summary should be requested for inclusion with the SAE documentation. In case of death, the investigator must make every effort to obtain a copy of the death certificate to submit to the Sponsor. When submitting copies of documentation, all participant identifying information must be redacted and only the unique participant number will be used to label the forms for identification purposes. All relevant documents in the local language should be summarized in English on the Case Report Form.

For any event where there is suspicion that the Omnipod 5 device is involved, the investigator will return the device for evaluation when possible.

9.12 Safety Oversight

The Medical Monitor will review all adverse events and adverse device events that are reported during the study. SAEs will typically be reviewed within 24-hours of reporting. Upon receipt of the SAE Report Form, the Medical Monitor will determine whether the event is unanticipated based on the investigator brochure (IB).

A listing of all AEs will be reviewed periodically by the Medical Monitor as part of routine safety signal detection.

10 STOPPING CRITERIA

10.1 Participant Discontinuation of Study Participation

In the case of a USADE for Intervention group participants, the Medical Monitor will determine if the use of the investigational device will be suspended while the problem is diagnosed. The use of the investigational device may continue if the Medical Monitor believes the event is explainable, unlikely to reoccur and that it is safe for the participant to continue using the device. Alternatively, the Medical Monitor may request the study participant, or all study participants, to stop using the investigational device or to only use in Manual Mode. Should Intervention group study participants be required to stop using the study device or to only use in Manual Mode due an USADE, use of the study device or Automated Mode will not be restarted until approval is received from the regulatory authorities.

Use of the investigational device by a participant will be discontinued if any of the following occur:

- The investigator, sponsor, or Medical Monitor believes it is unsafe for the participant to continue in the study for any reason. This could be due to the development of a new medical condition or worsening of an existing condition; or participant behavior contrary to the indications for use of the device that imposes on the participant's safety.
- The participant requests that the treatment be stopped
- Participant pregnancy
- Two distinct episodes of DKA as defined above
- Two distinct severe hypoglycemia events as defined above
- One episode of DKA and one severe hypoglycemia event as defined above

An additional requirement for continued study device use following a single DKA or severe hypoglycemia event will be that (1) the site investigator believes that the event is explainable, unlikely to recur, and that it is safe for the participant to continue to use the system and (2) the Medical Monitor concurs. If the Medical Monitor determines that the occurrence of the event indicates that it is not safe for the participant to continue to use the system, use will be discontinued, and the participant will be withdrawn from the study.

10.2 Criteria for Suspending or Stopping Overall Study

Error! Reference source not found. For unanticipated adverse device effects (USADEs), the Study Physician, together with the Medical Monitor per the Safety Management Plan (SMP), will determine whether the study should proceed or not based upon risk of additional serious adverse events and the underlying root cause analysis of the USADE.

Study activities could be similarly suspended if the manufacturer of any component of the investigational study device requires stoppage of device use for safety reasons (e.g., product recall).

The affected study activities may resume if the underlying problem can be corrected by a protocol or system modification that will not invalidate the results obtained prior to suspension.

The Study Physician and Medical Monitor may recommend suspension of study activities or stoppage of the study if deemed necessary based on the totality of safety data available.

10.3 Safety Signal Detection

Selected data from this study will be reviewed periodically to detect as early as possible any safety concern(s) related to the device so that Investigators, clinical study participants, regulatory authorities, and IRBs/IECs will be informed appropriately and as early as possible.

The Medical Monitor will conduct adjudication of any events of DKA or severe hypoglycemia or any additional events as requested by the Sponsor. The specified events will be adjudicated to determine:

- event relatedness to the study procedures and/or the devices (participant's own insulin pump, study CGM and Omnipod 5)
- whether an adverse event is unanticipated

The adjudication decision of the Medical Monitor will be used for the final classification of events, including relatedness to the study procedures and/or the devices, for the determination of safety endpoints and for all regulatory reports, product labeling, and publications or presentations.

Detailed roles and responsibilities of the Study Physician and Medical Monitor are described in the SMP.

11 STATISTICAL CONSIDERATIONS

11.1 Primary Endpoint and Hypotheses

The primary endpoint is per-participant percentage of time in range (TIR) 70-180 mg/dL as measured by study CGM and comparing the Intervention group to the Control group during the 13-week randomized period. The null hypothesis is that the mean percentage of TIR 70-180 mg/dL in the Intervention group is equal to the mean percentage of TIR 70-180 mg/dL in the Control group during the 13 weeks. The alternative hypothesis is that the mean percentage of TIR 70-180 mg/dL in the Intervention group is not equal to the mean percentage of TIR 70-180 mg/dL in the Control group during the 13 weeks.

Formally, the null and alternative hypotheses for the primary efficacy endpoint are:

H_0: $\mu_I - \mu_C = 0$

HA: $\mu_I - \mu_C \neq 0$

Where μ_I and μ_C are the population means of per-participant percentage of TIR 70-180 mg/dL as measured by the study CGM during the 13 weeks in the Intervention and Control groups, respectively.

The primary endpoint will be analyzed with a linear mixed effects model with TIR 70-180 mg/dL during the 13-weeks as the outcome. The full model specification will be described in the SAP.

11.2 Secondary Endpoints and Hypotheses

The following secondary per-participant endpoints will be evaluated and compared in the Intervention group vs. Control group at the end of the 13-week randomized period:

- Percentage of time <54 mg/dL (non-inferiority)
- Percentage of time >180 mg/dL
- Mean glucose
- Change from baseline in A1C
- Percentage of time < 70 mg/dL
- Change from baseline in Type 1-Diabetes Distress Scale (T1-DDS) total score at 13 weeks
- Change from baseline in Hypoglycemia Confidence Scale (HCS) total score at 13 weeks
- Change from baseline in Diabetes Quality of Life-brief (DQOL-brief) total score at 13 weeks

Secondary Endpoints will be tested in a hierarchical fashion.

The null and alternative hypotheses for the secondary endpoints are as follows:

<u>Percentage of time < 54 mg/dL (non-inferiority):</u>

H0: $\mu_I - \mu_C \geq 1\%$

HA: $\mu_I - \mu_C < 1\%$

Where μ_I and μ_C are the population means of percentage of time < 54 mg/dL during the 13 weeks in the Intervention and Control groups, respectively. The non-inferiority margin is 1%. If the upper bound of the two-sided 95% confidence interval for the difference (μ_I

minus μ_C) is <1%, non-inferiority will be established. If the upper bound of the two-sided 95% confidence interval for the difference (μ_I minus μ_C) is <0%, superiority of the Intervention group compared to the Control group will be established.

Percentage of time >180 mg/dL:

H0: $\mu_I - \mu_C = 0$

HA: $\mu_I - \mu_C \neq 0$

Where μ_I and μ_C are the population means of percentage of time >180 mg/dL during the 13 weeks in the Intervention and Control groups, respectively.

Mean glucose:

H0: $\mu_I - \mu_C = 0$

HA: $\mu_I - \mu_C \neq 0$

Where μ_I and μ_C are the population means of mean glucose during the 13 weeks in the Intervention and Control groups, respectively.

Change from baseline in A1C:

H0: $\mu_I - \mu_C = 0$

HA: $\mu_I - \mu_C \neq 0$

Where μ_I and μ_C are the population means of change from baseline in A1C after 13 weeks in the Intervention and Control groups, respectively.

Percentage of time < 70 mg/dL:

H0: $\mu_I - \mu_C = 0$

HA: $\mu_I - \mu_C \neq 0$

Where μ_I and μ_C are the population means of percentage of time < 70 mg/dL during the 13 weeks in the Intervention and Control groups, respectively.

Change from baseline in Type 1-Diabetes Distress Scale (T1-DDS) total score at 13 weeks:

H0: $\mu_I - \mu_C = 0$

HA: $\mu_I - \mu_C \neq 0$

Where μ_I and μ_C are the population means of change from baseline in T1-DDS total score after 13 weeks in the Intervention and Control groups, respectively.

If change from baseline in T1-DDS total score after 13 weeks is found to be statistically significantly different in the Intervention group compared to the Control group, the proportion of subjects in each treatment group achieving an improvement of ≥~~≥2~~ 0.19 points (MCID) in the T1-DDS total score after 13 weeks will also be compared. Those hypotheses are stated as:

H0: $\pi_I - \pi_C = 0$

HA: $\pi_I - \pi_C \neq 0$

Where π_I and π_C are the proportion of subjects achieving an improvement of 0.19 ~~≥2~~ points (MCID) in the T1-DDS total score after 13 weeks in the Intervention and Control groups, respectively.

Change from baseline in Hypoglycemia Confidence Scale (HCS) total score at 13 weeks:

H0: $\mu_I - \mu_C = 0$

HA: $\mu_I - \mu_C \neq 0$

Where μ_I and μ_C are the population means of change from baseline in HCS total score after 13 weeks in the Intervention and Control groups, respectively.

If change from baseline in HCS total score after 13 weeks is found to be statistically significantly different in the Intervention group compared to the Control group, the proportion of subjects in each treatment group achieving a score of ≥3 points in the HCS total score after 13 weeks will also be compared. Those hypotheses are stated as:

H0: $\pi_I - \pi_C = 0$

HA: $\pi_I - \pi_C \neq 0$

Where π_I and π_C are the proportion of subjects achieving a score of ≥3 points in the HCS total score after 13 weeks in the Intervention and Control groups, respectively.

Change from baseline in Diabetes Quality of Life-brief (DQOL-brief) total score at 13 weeks:

H0: $\mu_I - \mu_C \equiv 0$

HA: $\mu_I - \mu_C \neq 0$

Where μ_I and μ_C are the population means of change from baseline in DQOL-brief total score after 13 weeks in the Intervention and Control groups, respectively.

If change from baseline in DQOL-brief total score after 13 weeks is found to be statistically significantly different in the Intervention group compared to the Control group, the proportion of subjects in each treatment group achieving a clinically meaningful improvement in the DQOL-brief total score after 13 weeks will also be compared. Those hypotheses are stated as:

H0: $\pi_I - \pi_C = 0$

HA: $\pi_I - \pi_C \neq 0$

Where π_I and π_C are the proportion of subjects achieving a clinically meaningful improvement (defined as ≥0.5*standard deviation of change from baseline in DQOL-brief total score at 13 weeks) in the DQOL-brief total score after 13 weeks in the Intervention and Control groups, respectively.

Secondary endpoints will be analyzed using linear mixed effect models. The full model specifications will be described in the SAP.

11.3 Exploratory Endpoints

The following additional endpoints will be evaluated and compared in the Intervention group vs. Control group at the end of the 13-week randomized period:

- Proportion of participants with A1C <7%
- Proportion of participants with A1C <8%
- Proportion of participants with ≥1% improvement in A1C from baseline
- Proportion of participants with ≥10 relative percentage point improvement in A1C from baseline
- Proportion of participants with either ≥1% improvement in A1C from baseline OR ≥10 relative percentage point improvement in A1C from baseline
- Change from baseline in Body Mass Index (BMI)
- Change from baseline in total daily insulin (TDI) (units/kg)
- Additional CGM-derived endpoints, such as coefficient of variation, time above range >250 mg/dL, percentage of time < 54 mg/dL (superiority), TIR during daytime and nighttime hours
- Number of episodes of severe hypoglycemia
- Number of episodes of DKA

11.4 Patient-Reported Outcomes

The following questionnaires will be used to evaluate general and disease-specific quality of life, and device usability. Results will be assessed at 13 weeks compared to baseline (Intervention and Control group).

- Clarke hypoglycemia awareness questionnaire - Used to assess impaired awareness of hypoglycemia
- EQ-5D-3L – Used to measure quality of life
- T1-DDS[1] – Used to measure four critical dimensions of distress
- DQOL-brief[2] – Used to assess the relative burden of an intensive diabetes treatment regimen

- DIDP – Used to assess the perceived impact of diabetes in physical health, finances, relationships with family/friends, leisure activities, work/studies and emotional well-being
- HCS[3] –Used to measure hypoglycemia unawareness, hypoglycemia frequency, severity, and impact
- PSQI – Used to measure sleep disturbance and usual sleep habits
- SUS – Used to measure usability of a system
- INSPIRE – Used to evaluate the impact of AID systems on the psychosocial functioning and quality of life

Any endpoint that is not listed as a Primary, Secondary, or Exploratory endpoint will be treated as exploratory.

11.5 Sample Size

The study is powered at 90% to detect a between-group difference of 10% in TIR 70-180 mg/dL and assuming a standard deviation of 16.5% in each group. Under these assumptions and with 2:1 Intervention:Control randomization, a total sample size of 131 participants is required (87 Intervention, 44 Control). To allow for pre-randomization attrition of up to 15%, and post-randomization attrition of up to 22.9%,a total sample size of up to 200 will be enrolled to obtain 170 randomized participants with 131 participants completing the 13 weeks. The anticipated difference in TIR 70-180 mg/dL was projected from the OP5 pivotal study. PASS 2022 was used for sample size calculations.

11.6 Analysis Sets

The following analysis sets are planned for the study:

11.6.1 ITT (Intention to Treat) Analysis Set

The ITT analysis set includes all participants that are enrolled in the study. All safety analyses will be based on the ITT analysis set.

11.6.2 mITT (modified Intention to Treat) Analysis Set

The modified Intention to Treat (mITT) analysis set is a subset of the ITT analysis set. The mITT analysis set will consist of all participants who have been randomized. The mITT analysis set will be used as the primary analysis for the primary and secondary endpoints and for other clinical outcome data.

11.7 PP (Per-Protocol) Analysis Set

The Per-Protocol (PP) analysis set is a subset of the mITT analysis set. Participants will be included in the PP analysis set if they have a minimum of 80% system use as measured by the study CGM (control group) or Omnipod 5 (intervention group) during the 13-week randomized period over a minimum duration of 10 weeks and have completed the study without major protocol deviations. The PP analysis set will be used as supportive analysis for the endpoints. The following will be considered major protocol deviations:

- Major inclusion/exclusion criterion deviation

- Significant protocol non-compliance that may confound the study objective data (e.g., use of prohibited medications, not using control group pump for prolonged period)

The list of participants excluded from the PP analysis set will be determined prior to analysis while blinded to treatment group. If the PP analysis set does not differ from the mITT analysis set, separate analyses will not be presented.

11.8 Analysis of Primary and Secondary Endpoints

The primary endpoint will be tested for statistical significance in the mITT analysis set at a two-sided significance level of.5%. Hypothesis testing for the secondary endpoints will commence if and only if the primary endpoint is found to be statistically significant (i.e. two-sided p-value ≤ 0.05). Strict control of Type I error will be maintained with a hierarchical testing procedure, with secondary endpoints tested in the following order:

- Percentage of time <54 mg/dL (non-inferiority)
  - If the upper bound of the two-sided 95% confidence interval for the difference (μ_I minus μ_C) is <1%, non-inferiority will be established. If the upper bound of the two-sided 95% confidence interval for the difference (μ_I minus μ_C) is <0%, superiority of the Intervention group compared to the Control group will be established.
- Percentage of time >180 mg/dL
- Mean glucose
- Change from baseline in A1C
- Percentage of time < 70 mg/dL
- Change from baseline in Type 1-Diabetes Distress Scale (T1-DDS) total score at 13 weeks
  - If change from baseline in T1-DDS total score at 13 weeks is found to be statistically significantly different in the Intervention group compared to the Control group, the proportion of subjects in each treatment group achieving an improvement of ≥0.19 points (MCID) in the T1-DDS total score at 13 weeks will also be compared.
- Change from baseline in Hypoglycemia Confidence Scale (HCS) total score at 13 weeks
  - If change from baseline in HCS total score at 13 weeks is found to be statistically significantly different in the Intervention group compared to the Control group, the proportion of subjects in each treatment group achieving a score of ≥3 points in the HCS total score at 13 weeks will also be compared.
- Change from baseline in Diabetes Quality of Life-brief (DQOL-brief) total score at 13 week
  - If change from baseline in DQOL-brief total score at 13 weeks is found to be statistically significantly different in the Intervention group compared to the Control group, the proportion of subjects in each treatment group achieving a clinically meaningful improvement (defined as ≥0.5*standard deviation of change from baseline in DQOL-brief total score at 13 weeks) in the DQOL-brief total score at 13 weeks will also be compared.

Each endpoint with a two-sided p-value of ≤0.05 (equivalent to one-sided p-value ≤ 0.025) is considered to be met until a secondary endpoint with a two-sided p-value of

>0.05 (equivalent to one-sided p-value > 0.025) is encountered. That secondary endpoint, and all subsequent secondary endpoints, are considered to not be met irrespective of their observed p-values.

There will be no formal hypothesis testing for the exploratory endpoints.

The primary, secondary, and additional endpoints will be summarized for the mITT and PP analysis sets. If the PP analysis set does not differ from the mITT analysis set, separate analyses will not be presented.

12 PERCENTAGE OF TIME ENDPOINTS

The primary endpoint and the secondary endpoints that summarize time in specific glycemic ranges will be calculated from device data outputs as follows:

$$100 \times \frac{\#\ of\ CGM\ records\ in\ range}{\#\ of\ evaluable\ CGM\ records} = \%\ of\ time$$

12.1 Subgroup Analyses

Summary statistics will be stratified by time points of interest (e.g., day vs. night, overall). Any additional subgroup analyses will be detailed in the SAP.

12.2 Additional Data Analyses

CGM and Omnipod 5 device data will be made available to Sponsor representatives for periodic reviews. Reviews of the controller data will be conducted to identify any anomalies and to confirm the algorithm appears to be functioning as expected. These reviews, including any findings, will be documented. Unless potential safety concerns are identified, the results of such reviews will not be shared with study sites or participants and thus, will not impact study endpoints. Should a potential safety concern be identified, sites may be notified as appropriate to ensure participant safety and measures may be taken to address the issue such as, but not limited to, changes to the protocol and/or device. Any resulting device deficiencies will be reported, if applicable. A brief summary of the controller data reviews will be included in the final clinical study report.

12.3 Safety Analyses

12.3.1 Evaluation of Adverse Events

All adverse events reported over the course of the study will be summarized and tabulated by study phase (standard therapy or 13-week follow-up), event category, seriousness, severity, and relationship to the study procedure and the devices. For the purposes of summarization, an event will be considered "Related" if the relationship was deemed as "Possibly Related" or "Related". In cases where the same event is reported more than once per participant, the event will only be counted once in the incidence table(s).

Adverse events leading to death or to discontinuation from the study will be listed separately. A listing of all adverse events will be provided.

12.3.2 Evaluation of Device Deficiencies

Device deficiencies will be tabulated and listed in a manner similar to the methods described for adverse events. Any device deficiency leading to an AE or to study termination will be listed separately.

12.3.3 Episodes of Severe Hypoglycemia and DKA

The number of severe hypoglycemia and DKA adverse events, and the number and percent of subjects with at least one event in each group will be summarized. Statistical testing will be performed for the rate of SH (and DKA) if there are ≥5 events (of SH or DKA, respectively) combined across both treatment groups. The rates will be calculated as the number of events per 100 person years.

12.4 Baseline Characteristics

The distribution of each baseline characteristic or demographic parameter of interest (such as age, gender, medical history, etc.) will be presented. Data on all enrolled participants will be presented. Continuous variables will be summarized using count, mean, median, standard deviation, and range. Categorical variables will be summarized using counts and percentages.

12.5 General Statistical Methods

Standard statistical methods will be employed to analyze all data. Data collected in this study will be presented using summary tables and participant data listings. Unless otherwise noted, all p-values will be considered significant at a two-sided significance level of 5%. Continuous variables will be summarized using descriptive statistics, including count, mean, median, standard deviation (SD), minimum and maximum. Where appropriate, 95% two-sided confidence intervals for the means or medians will be presented. If the observed data are found not to follow a normal distribution, appropriate non-parametric methods may be employed. Categorical variables will be summarized by frequencies and percentages. Unless explicitly stated otherwise, percentages will utilize a denominator corresponding to the number of unique participants.

12.6 Missing Data

All practical monitoring and follow-up steps will be taken to ensure complete and accurate data collection.

Due to the nature of the data and study design, it is anticipated that all randomized subjects will contribute some CGM data post-randomization. Hence, it is possible that there will be no need for imputation of missing values for the CGM endpoints. A subject will be included in analysis of CGM endpoints in the mITT analysis set only if the subject provides at least seven days' worth of sensor readings during the course of 13 weeks. This is equivalent to 2016 readings, assuming CGM readings are taken at approximately every five minutes for a total of 288 readings per day. No additional imputations for missing data are planned for the primary endpoint, and secondary endpoints involving CGM data. Missing records (i.e. gaps in data) will not be imputed for either the intervention or control group.

CGM values for other reasons will not be imputed.

It is likely that at least some subjects do not contribute data for the A1C and patient-reported outcome endpoints (e.g., due to early withdrawal).

For the main analysis of A1C and patient-reported outcomes, missing values for the subjects in the mITT analysis set will be imputed using the subject's last known A1C/ePRO value if collected within the analysis window (such as during Early Withdrawal visit). The analysis windows are assigned as follows:

- A1C à 13±2 weeks from start of the 13-week randomized period
- PROs à 13±5 weeks from start of the 13-week randomized period

Questionnaire scoring will follow the scoring guidelines; PRO scores either at baseline or at 13 weeks that are missing for other reasons (e.g., due to unanswered questions) will not be imputed. No imputation for missing data will be included in the analyses based on Per Protocol analysis set. Additional sensitivity analyses will be detailed in the SAP.

12.7 Statistical Software

The statistical software package SAS® 9.4 or later will be used for all the data derivations, summarization, data listings and statistical analyses. Additional software such as Splus or R may be used for graphics or validation as appropriate.

Additional details regarding statistical analyses will be provided in the SAP which will be prepared prior to data analysis. If discrepancies exist between the protocol and the SAP, the SAP will prevail. Any deviations from the finalized SAP will be described in the final study report.

13 DATA HANDLING AND QUALITY ASSURANCE

Data in this study will be collected on Electronic Case Report Forms as well as via electronic device outputs.

13.1 Electronic Case Report Forms (eCRFs)

Study data are collected through a combination of participant electronic CRFs (eCRFs) and electronic device data files. eCRF Data will be recorded in a 21 CFR Part 11 compliant database that will reside on a central server accessible via the Internet.

Electronic data files contain the primary source data for study devices. When data are directly collected in the eCRFs, this will be considered source data. When data is not directly collected in the eCRFs, electronic or paper documents containing source data that is transcribed into the eCRF are the source.

The investigator is responsible for the accuracy and completeness of data reported on the eCRFs. Each set of participant eCRFs must be reviewed and signed by the investigator in the Electronic Data Capture (EDC) system. The investigator also agrees to maintain accurate source documentation supporting the data. When pertinent supportive information is available for data entered directly into the eCRFs, this supporting documentation will also be maintained. Source documents may include chart notes, laboratory reports, images, study specific source worksheets, eCRFs, device data files, etc.

13.2 Electronic Device Outputs

13.2.1 Omnipod 5 System Data

For the Intervention group, the study will collect insulin delivery data from the Omnipod 5 System. All insulin delivery and CGM data from the Omnipod 5 System will be stored on the device and exported to the Insulet Cloud. Data will be saved in a compatible format that will be extractable for statistical analysis purposes.

13.2.2 CGM Data

The study will collect CGM data from the CGM device for all participants. All CGM data will be stored and exported to the Cloud. CGM data will be saved in a compatible format that will be extractable for statistical analysis purposes.

13.2.3 BG/Ketone Meter Data

This study will also utilize measurements from a BG and ketone meter. BG or Ketone meter data, in any format, may be uploaded to the database if requested.

13.2.4 Participant Identifiers

All data used in the analysis and reporting of the study will be without identifiable reference to the participant. Only the unique participant number will be used to identify participant data submitted to the Sponsor, and only the investigating clinical site will be able to link the unique participant ID to the participant's name.

13.2.5 Monitoring Responsibilities

This study will be monitored for compliance with the protocol and applicable regulatory requirements. A study specific monitoring plan will specify the minimum frequency, scope, and general conduct of monitoring visits as well as identify any relevant study-specific monitoring responsibilities.

Monitors for this study will be qualified by education, experience and training. The monitor will report to the Sponsor any non-compliance with the protocol, applicable regulations, or any conditions imposed by the IRB or local regulatory authority. If compliance cannot be secured, device shipments to the Investigator may be discontinued and the Investigator's participation in the study terminated.

Investigators and clinical site coordinators are expected to make source files and other records and reports available to the monitors as required.

13.2.6 Inspection of Records

The Sponsor or its designee may perform quality assurance site and study file audits. Investigators and institutions involved in the study will permit trial-related monitoring, audits, IRB/EC review, and regulatory inspection by providing direct access to all study records. In the event of an audit or inspection, the investigator agrees to allow the Sponsor, representatives of the Sponsor, or regulatory authorities access to all study records.

The investigator should promptly notify the Sponsor of any study inspections scheduled by the regulatory authorities and promptly forward copies of any audit reports received to the Sponsor.

13.2.7 Study Record Retention

Records and reports will be archived according to local regulations and in accordance with maximum period of time permitted by institution or for a minimum of two years after the later of either the completion/termination of the study or the date of market approval for the indication being studied. They may be discarded only upon approval from the Sponsor. The Principal Investigator must contact the Sponsor before destroying any records and reports pertaining to the study to ensure that they no longer need to be retained. In addition, the Sponsor must be contacted if the investigator plans to leave the investigational site to ensure that arrangements for a new investigator or records transfer are made prior to investigator departure.

13.2.8 Device Accountability

Investigators will be responsible for device accountability, reconciliation, and records maintenance throughout the course of the investigation. Accountability records will include receipt, use and final disposition of study supplied devices.

Study devices must be stored according to the conditions set forth for the device on the label in a controlled, locked area. All device shipment records (packing lists, etc.) must be maintained at the clinical site.

The study monitor will verify accountability of the study devices during routine monitoring visits to the clinical site.

14 STUDY ETHICS AND CONDUCT

14.1 Role of the Sponsor

As the Sponsor of this clinical study, Insulet has the overall responsibility for the conduct of the study, including assurance that the study meets the requirements of the appropriate regulatory bodies. In this study, the Sponsor will have certain direct responsibilities and may delegate certain study tasks to the Contract Research Organization (CRO).

14.2 Ethical Conduct of the Study

The investigation will be conducted according to the ethical principles that have their origin in the Declaration of Helsinki and are consistent with GCP and the applicable regulatory requirements with the rights, safety, and well-being of the trial participant the most important consideration. The investigator will conduct all aspects of this study in accordance with all state, and local laws or regulations.

14.3 International Review Board (IRB) and Ethics Committees (EC)

Regulations require that approval/favorable opinion be obtained from an IRB/EC for protocol, informed consent and any written information to be provided to the participants prior to participation of participants in research studies. Prior to participant enrollment, IRB/EC approval letter must be submitted to the Sponsor. Documentation of all IRB/EC

approvals will be maintained by the clinical site and will be available for review by the Sponsor or its designee.

All IRB/EC approvals should be signed by the IRB/EC chairperson or designee and must identify the IRB/EC by name and address, the clinical protocol by title and/or protocol number, and the date approval was granted.

The Investigator is responsible for submitting and obtaining initial and continuing review of the trial at intervals not exceeding 1 year or as otherwise directed by the IRB/EC. The investigator must supply the Sponsor, or its designee written documentation of continued review of the study.

14.4 Informed Consent

A written informed consent in compliance with applicable regulations must be obtained from each participant prior to participating in the study or performing any unusual or non-routine procedure that involves risk to the participant. An informed consent form (ICF) template will be provided by the Sponsor or designee to investigative clinical sites. If any institution-specific modifications to study-related procedures are proposed or made by the clinical site, the consent must be reviewed by the Sponsor prior to IRB/EC submission. Once reviewed, the consent will be submitted by the investigator to their IRB/EC for review and approval prior to the start of the study.

Before recruitment and enrollment, each prospective participant will be given a full explanation of the study and be given ample time to read the approved ICF and ask questions. Once the investigator or designee is assured that the participant understands the implications of participating in the study, the participant will be asked to give consent to participate in the study by signing the ICF.

The investigator or designee shall provide a copy of the signed ICF to the participant. The original form shall be maintained in the participant binder at the clinical site.

14.5 Confidentiality

All information and data sent to the Sponsor concerning study participants or their participation in this trial will be considered confidential. Only authorized personnel will have access to these confidential files. All records will be kept in secure storage areas and on password-protected computers.

This includes, but is not limited to the following:

- Participants will be identified on all eCRFs by a unique participant ID
- eCRFs are confidential documents and will only be available to the Sponsor (including delegates, such as CRAs), Medical Monitor, CRO, the investigator and study staff, and if requested, to the IRB/EC or regulatory authorities. The investigator will maintain, as part of the investigation file, a list identifying all participants entered into the study.

All laboratory specimens, evaluation forms, reports, and other records will be identified in a manner designed to maintain participant confidentiality. Clinical information will not be released without the written permission of the participant, except as necessary for monitoring and auditing by the Sponsor, its designee, the regulatory authorities, or the IRB/EC.

The investigator and all clinical site staff involved in this study may not disclose (or use for any purpose other than performance of the study), any data, record, or other unpublished confidential information disclosed to those individuals for the purpose of the study. Prior written agreement from the Sponsor or its designee must be obtained for the disclosure of any said confidential information to other parties.

14.6 Modification of the Protocol

Any changes in this research activity, except those necessary to remove an apparent immediate hazard to the participant, must be reviewed and approved by the Sponsor. The protocol amendment(s) must be signed by the investigator and approved by the IRB/EC before implementation. The protocol amendment(s) will be filed with the appropriate regulatory agency(s) having jurisdiction over the conduct of the study and may require approval prior to implementation.

Substantial changes will require approval from the Sponsor and IRB/EC prior to implementation.

14.7 Protocol Deviations

The investigator will not deviate from the protocol except in medical emergencies or in unforeseen, isolated instances where minor changes are made that will not increase the participant's risk or affect the validity of the trial. In medical emergencies, prior approval for protocol deviations will not be required, but the Sponsor must be notified within 2 working days of the incident. Periodic monitoring of protocol compliance will be performed for each clinical site. The Sponsor has the right to suspend enrollment at clinical sites deemed to have excessive protocol compliance issues.

All deviations related to study inclusion or exclusion criteria, conduct of the study, participant management or participant assessment must be appropriately documented and reported. Other protocol deviations to be considered include non-adherence to the protocol that results in a significant additional risk to the participant.

The investigator must document and explain any protocol deviation in the participant's source documentation. The IRB/EC should be notified of all protocol deviations in a timely manner. Protocol deviations should be reported to the IRB/EC periodically, according to their requirements. Deviations will also be reviewed by the monitor during clinical site visits and those observations may be discussed with the investigator.

The Sponsor will evaluate circumstances where the investigator deviates from the study protocol and will retain the right to remove either the investigator or the investigational clinical site from the study.

14.8 Study Reporting Requirements

By participating in this study, the investigator agrees to submit SAE reports according to the timeline and method outlined in this protocol. In addition, the investigator agrees to submit annual reports to his/her IRB/EC as appropriate.

Upon completion or termination of the study, the principal investigator (PI) must submit a final written report to the Sponsor and IRB/EC. The report must be submitted within 3 months (90 days) of completion or termination of the trial.

The Sponsor will submit all reports required by the appropriate regulatory authorities, including unanticipated adverse device effects, SAE, withdrawal of IRB/EC approval, list of current investigators, annual progress reports, recall information, final reports and protocol deviations.

14.9 Selection of Investigators

The Sponsor will select qualified investigators, ship devices only to participating investigators, obtain a signed Investigator's Agreement and provide all investigators with the information and training necessary to conduct the study.

14.9.1 Financial Disclosure

Investigators and sub-investigators are required to provide financial disclosure information to allow the Sponsor to submit the complete and accurate certification or disclosure statements required under 21 CFR 54. In addition, the investigator must notify the Sponsor promptly of any relevant changes that occur during the course of the study, at the completion of the study, and 1 year following the completion of the study.

14.9.2 Investigator Documentation

Prior to beginning the study, the investigator will be asked to provide the following essential documents, including but not limited to:

- An investigator-signed Investigator Agreement page of the protocol
- An investigator-signed Investigator Agreement page of the Investigator Brochure
- An IRB/EC approved informed consent, samples of clinical site advertisements for recruitment for this study, and any other written information regarding this study that is to be provided to the participant
- IRB/EC approval of the investigator, protocol, and acknowledgement of the user guide
- Curricula vitae (CV) for the PI and each investigator participating in the study. Current licensure must be noted on the CV or a copy of the license provided. CVs must be signed and dated by the investigators within 1 year of study start-up, indicating that they are accurate and current.
- Financial disclosure information (as stated above) and a commitment to promptly update this information if any relevant changes occur
- Investigator Agreement Form signed agreement to conduct the study in accordance with the relevant, current Protocol, and applicable regulatory authority and IRB/EC regulations
- Laboratory certifications and normal ranges for any local laboratories used by the clinical site.

14.10 Clinical Site Training

The training of appropriate clinical site personnel will be the responsibility of the Sponsor or its designee. To ensure proper device usage, uniform data collection, and protocol

compliance, the Sponsor or designee will present formal training sessions to relevant clinical study site personnel. Clinical study personnel trained by the Sponsor may also train additional clinical study personnel at their site. The Sponsor reserves the right to enforce retraining for clinical sites who have demonstrated study or procedure compliance issues. Protocol-specific training will occur for all research personnel and key ancillary staff who will be involved in participant care.

14.11 Device Use

The Omnipod 5 System consists of the following primary components: The Pod (insulin infusion pump with SmartAdjust technology), Omnipod 5 App(installed on the Insulet-provided Controller), and the Dexcom G6 CGM (sold separate and manufactured by Dexcom).

The Pod and Controller are intended for single use only. The Controller will be returned to the Sponsor after completion of the study.

The Dexcom G6 CGM sensor (the component of the system that enters the skin) and the Dexcom G6 CGM transmitter (the component of the system that attaches to the sensor to transmit the signal) will all be single use only in this study.

New blood glucose meters, ketone meters, CGM sensors, and transmitters will be dispensed to each participant. Any unused blood glucose meters, ketone meters, CGM sensors, and transmitters will be returned to Insulet.

14.12 Device Returns

Any unused or damaged investigational devices or investigational devices related to a suspected deficiency or adverse event must be returned to the study Sponsor. To initiate the return, the clinical site will contact the Sponsor representative and provide the following information:

- Part number/Lot number
- Quantities
- Tracking number

14.13 Policy for Publication and Presentation of Data

All data and results and all intellectual property rights in the data and results derived from the study will be the property of the study Sponsor, Insulet.

14.14 Sponsor or Regulatory Agency Termination of the Study

Although the Sponsor intends to complete the study, the Sponsor reserves the right to stop the study at any time for clinical or administrative reasons, or if required by the local regulatory authority, with suitable written notice to the investigators and regulatory authorities as appropriate.

Similarly, investigators may withdraw from the study by providing written notification to the Sponsor within 30 days of intent to withdraw. However, the Sponsor and investigators will be bound by their obligation to complete the follow-up of participants already enrolled in the trial. Participants must be followed according to the clinical protocol and information obtained during participant follow-up shall be reported on the eCRF.

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