Summary of Safety and Clinical Performance

Tandem Mobi Insulin Pump with Control-IQ+ Technology with Tandem Mobi Mobile Application and Tandem Mobi 2 mL Cartridge

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This Summary of Safety and Clinical Performance (SSCP) is intended to provide public access to an updated summary of the main aspects of the safety and clinical performance of the device.

The SSCP is not intended to replace the User Guide as the main document to ensure the safe use of the device, nor is it intended to provide diagnostic or therapeutic suggestions to intended users or patients.

The following summary information is intended for healthcare professionals:

1. Device Identification and General Information

Device Trade Name	Tandem Mobi Insulin Pump with Control-IQ+ Technology Tandem Mobi 2mL cartridge Tandem Mobi Mobile App
Manufacturer's Name and Address	Tandem Diabetes Care, Inc. 12400 High Bluff Drive San Diego, CA 921230 USA
SRN	US-MF-000031791
Basic UDI-DI	Tandem Mobi Insulin Pump with Control-IQ+ Technology Basic UDI-DI: 00389152TF0018738ZJ Tandem Mobi 2mL Cartridge Basic UDI-DI: 0389152TF0009858CHN Tandem Mobi Mobile Application Basic UDI-DI: 0850018992TF-0011603KR
EMDN Codes	EDMN code for the Tandem Mobi Insulin pump is: Z1204021601 - PORTABLE INSULIN INFUSION INSTRUMENTS EMDN code for the Tandem Mobi 2mL cartridge is: Z1204021685 - PORTABLE MICROINFUSION INSTRUMENTS – CONSUMABLES EMDN code for the Tandem Mobi Mobile App is: Z12030382 – INFUSION INSTRUMENTS – SOFTWARE ACCESSORIES
Class/Classification Rule	Tandem Mobi insulin pump with Control-IQ+ technology: Class III per Rule 22 Tandem Mobi 2 mL Cartridge: Class IIa per Rule 2 Tandem Mobi Mobile App: Class III per Implementing Rule 3.3
Year When First CE Certificate Issued	Device is not CE marked.
Authorized Representative	MDSS GmbH Schiffgraben 41 Hannover 30175, Germany DE-AR-000005430
Notified Body	BSI Group Netherlands BV NB 2797

2. Intended Purpose of the Device and Any Indications, Contraindications, and Target Populations

Intended Purpose	The Tandem Mobi insulin pump with interoperable technology (the pump) is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ+ is intended for use with a compatible continuous glucose monitor (CGM) and the Tandem Mobi insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The Tandem Diabetes Care 2 mL cartridge is intended for use with the Tandem Mobi insulin pump for the Continuous Subcutaneous Delivery of Insulin (CSII). The Tandem Mobi mobile app allows a user to connect a compatible smartphone to the pump, using Bluetooth® wireless technology, to view data from the Tandem Mobi pump and perform pump functions directly on the user's smartphone. The Tandem Mobi mobile app also provides messages and alerts from the Tandem Mobi pump as push notifications on the user's smartphone. The Tandem Mobi mobile app can transmit pump and therapy data from the pump to the cloud as long as the user's smartphone is connected to the Internet.
Indications	Individuals diagnosed with diabetes mellitus, requiring insulin, that are two years of age and greater.
Intended Patient Populations	Persons 2 years of age and greater who require a total daily insulin dose of at least 5 units and who weigh at least 9 kilograms.
Contraindications	None.

3. Device Description

3.1. Device Overview

The Tandem Mobi Insulin Pump with Control-IQ+ Technology

The Tandem Mobi insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices.

Control-IQ+ technology is intended for use with a compatible continuous glucose monitor (CGM) and the Tandem Mobi insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold.

Tandem 2 mL Cartridge Accessory:

The Tandem Mobi 2 mL cartridge is intended for use with the Tandem Mobi insulin pump for the Continuous Subcutaneous Delivery of Insulin (CSII).

Tandem Mobi Mobile App Accessory:

The Tandem Mobi mobile app allows a user to connect a compatible smartphone to the pump, using Bluetooth® wireless technology, to view data from the Tandem Mobi pump and perform pump functions directly on the user's smartphone. The Tandem Mobi mobile app also provides messages and alerts from the Tandem Mobi pump as push notifications on the user's smartphone. The Tandem Mobi mobile app can transmit pump and therapy data from the pump to the cloud as long as the user's smartphone is connected to the Internet.

3.2. Previous Generations and Variants

Control-IQ+ technology, the latest version of the automated insulin delivery algorithm in the pump, allows for wider range of weight and TDI input, in addition to other changes to enhance performance for users with high basal rates compared to the original version of Control-IQ technology. Control-IQ+ technology also adds support for temporary basal rates and extended boluses up to 8 hours with Control-IQ+ active.

3.3. Description of Accessories

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

- USB Charging Pad, wall power USB adapter, USB cable for charging the pump's internal battery;
- Pump Case/Clip

3.4. Description of Other Devices Intended to be Used in Combination with the Device

The following devices are intended to be used in combination with the Tandem Mobi Insulin Pump with Control-IQ+ Technology with some commercially available from other manufacturers:

- Tandem Mobi 2 mL Cartridge
- Tandem Mobi Mobile App
- CGMs

4. Risks and Warnings

4.1. Residual Risks and Undesirable Effects

Qualitative data on side-effects and residual risks related to Control-IQ+ technology were identified through prospective randomized clinical trials on the t:slim X2 Insulin Pump with Control-IQ+ Technology, the equivalent device. See **Figure 1**, **Figure 2, Figure 3, Figure 4, and Figure 5** for a quantification of all risks associated with the t:slim X2 Insulin Pump with Control-IQ Technology (equivalent device) from pivotal clinical trials.

The following data represents the clinical performance of the Control-IQ™ technology in five prospective pivotal clinical studies. The first pivotal study (the DCLP3, participants (N=168, CIQ=112, SAP=56)) included participants ≥14 years old. A second pivotal study (the DCLP5, N=101, CIQ=78, SAP=23) included participants ≥6 years to 13 years old. A third pivotal study (PEDAP, N=102, CIQ=68, Standard Care=34) included participants ≥2 to <6 years old. In the first two studies, the t:slim X2 insulin pump with Control-IQ technology was compared to Sensor Augmented Pump (SAP) therapy alone (the control group). In the second study, Control-IQ technology was compared to the Standard Care (SC), which included multiple daily injections (MDI) and pump use.

The PEDAP trial was followed by a 3 month extension phase where all participants used Control-IQ+ technology. Additionally, high insulin use with Control-IQ+ technology was evaluated in 34 participants in the single-arm Higher-IQ trial. All participants in these studies used the Dexcom G6 CGM.

		Number of Events	
		Control-IQ (n=112)	SAP (n=56)
Total Number of Adverse Events		13	3
Adverse Events Related to Study Device			
	Ketosis (Infusion Site Failure)	3	0
	Hyperglycemia (Infusion Site Failure)	4	2
	Hyperglycemia (Defected Cartridge)	1	0
	Diabetic Ketoacidosis (Infusion Set Failure)	1	0
Adverse Effects Not Related to a Study Device			
	Hyperglycemia (User Error)	3	0
	Hyperglycemia (Respiratory Infection)	0	1
	Coronary Bypass Surgery	1	0
	Otitis Externa	1	0
	Concussion	1	0

Figure 1 DCLP3 Types and Number of Adverse Events By Treatment Group

		Number of Events	
		Control-IQ (n=78)	SAP (n=23)
Total Number of Adverse Events		16	3
Adverse Events Related to Study Device			
	Ketosis (Infusion Site Failure)	8	0
	Abscess at Sensor Site (CGM Sensor)	0	2
	Hyperglycemia (Defected Cartridge)	1	0
Adverse Effects Not Related to a Study Device			
	Hypoglycemia (User Error)	1	0
	Ketosis (User Error)	2	1
	Ketosis (Gastroenteritis)	1	0
	Hyperglycemia (User Error)	2	0
	Accidental Over-Delivery of Insulin (User Error)*	1	0
*One subject primed tubing while connected to body. This was a serious adverse event, requiring treatment in the emergency room for hypoglycemia prevention.			

Figure 2 DCLP5 Types and Number of Adverse Events By Treatment Group

		Number of Events	
		Control-IQ (n=68)	SC (n=34)
Total Number of Adverse Events		71	14
Severe Hypoglycemic (SH) Events*		2	1
Diabetic Ketoacidosis (DKA) Events†		1	0
Other Serious Adverse Events‡ (SAEs)		0	1
Other Adverse Events *N Events/N Participants*		68/40	12/9
	Hyperglycemia with or without Ketosis Related to Study Device	39/26	0
	Hyperglycemia with or without Ketosis Not Related to Study Device	12/9	8/7
	Hypoglycemia (not severe)	2/2	0/0
	Burn	1/1	0/0
	COVID-19	3/3	0/0
	Fall	1/1	0/0
	Fractured Finger	1/1	0/0
	Gastroenteritis	2/2	2/2
	Hematuria	1/1	O/O
	Medical Device Site Bleeding	1/1	0/0
	Skin Infection	3/2	0/0
	Streptococcal Sore Throat	1/1	0/0
	Upper Respiratory Infection	1/1	0/0
	Vomiting	0/0	2/1

**A severe hypoglycemic event is defined as a hypoglycemic event that a) required assistance of another person due to altered consciousness, and b) required another person to actively administer carbohydrate, glucagon, or other resuscitative actions.*
†*DKA events meeting DCCT criteria.*
‡*One participant in the SC group was hospitalized for an asthma flare.*

Figure 3 PEDAP Types and Number of Adverse Events By Treatment Group

		Number of Events	
		CLC-CLC (n=63)	SC-CLC (n=33)
Total Number of Adverse Events		46	29
Severe Hypoglycemic (SH) Events* *N Events/N Participants*		2/2	0/0
Other Serious Adverse Events† (SAEs) *N Events/N Participants*		1/1	0/0
Other Adverse Events *N Events/N Participants*		43/34	29/16
	Hyperglycemia with or without Ketosis Related to Study Device	20/18	8/8
	Hyperglycemia with or without Ketosis Not Related to Study Device	10/8	12/4
	Hypoglycemia (not severe)	1/1	0/0
	Allergy NOS	1/1	0/0
	Cellulitis	0/0	1/1
	COVID-19	3/3	0/0
	Fever	0/0	1/1
	Gastroenteritis	2/2	2/2
	Head Injury	0/0	1/1
	Influenza	1/1	0/0
	Laceration	0/0	1/1
	Pneumonia	1/1	0/0
	Skin Infection	1/1	2/2
	Upper Respiratory Infection	1/1	0/0
	Viral Syndrome	1/1	0/0
	Vomiting	1/1	1/1

**A severe hypoglycemic event is defined as a hypoglycemic event that a) required assistance of another person due to altered consciousness, and b) required another person to actively administer carbohydrate, glucagon, or other resuscitative actions.*
† One participant in the CLC-CLC group was hospitalized for muscle pain

Figure 4 PEDAP Extension Phase Types and Number of Adverse Events By Treatment Group

		Number of Events
		All Participants Used Control-IQ
Total Number of Adverse Events		38
Severe Hypoglycemic (SH) Events*		0
Diabetic Ketoacidosis (DKA) Events†		0
Other Serious Adverse Events‡ (SAEs)		1
Other Adverse Events *N Events/N Participants*		37/18
	Hyperglycemia with or without Ketosis Related to Study Device	1/1
	Hyperglycemia with or without Ketosis Not Related to Study Device	0/0
	Bronchitis	1/1
	Chronic Kidney Disease	1/1
	Cough	1/1
	COVID-19	2/2
	Dyslipidemia	1/1
	Hypertension	1/1
	Influenza	3/3
	Ligament Sprain	1/1
	Migraine	1/1
	Myalgia	1/1
	Nausea/Vomiting	2/2
	Oropharyngeal Pain	1/1
	Otitis Externa	1/1
	Otitis Media	2/2

Figure 5 Higher-IQ Types and Number of Adverse Events

How Potential Risks Have Been Controlled or Managed

Risks have been controlled and managed through device design, labeling, and patient training.

Residual Risks and Undesirable Effects

Many of the risks are common to insulin therapy in general. There are additional risks with use of the devices. Residual risks from using the devices include:

- Hypoglycemia from over-delivery of insulin.
- Hyperglycemia and ketosis possibly leading to Diabetic Ketoacidosis.
- Infection and signs of infection such as bleeding, pain, and skin irritation including redness at the site of insulin infusion.

- Allergic reaction or skin irritation due to patient allergy or sensitivity to adhesive from the infusion set used with the device or skin irritation due to patient having fragile or easily damaged skin.

Tandem Diabetes Care Inc. continuously collects post market surveillance data to ensure the continued safety and performance of the device. The Control-IQ Observational Study evaluated these risks, assessing the safety and effectiveness of the device in a real-world setting.

4.2. Warnings and Precautions

Below is a list of important warnings and precautions. Refer to the User Guide for the full list of warnings and precautions.

4.2.1. Summarized Warnings and Precautions for Patients*

- Control-IQ+ technology should not be used in anyone under the age of two years old. Control-IQ+ should also not be used in patients who require less than a total daily insulin dose of 5 units per day and should not be used by people who weigh less than 9 kilograms (20 pounds), as those are the required minimum values needed in order for Control-IQ+ to operate safely.
- ALWAYS be prepared to inject insulin with an alternative method if delivery is interrupted for any reason. Your pump is designed to deliver insulin reliably, but because it uses only rapid-acting insulin, you will not have long-acting insulin in your body. Failure to have an alternative method of insulin delivery can lead to very high BG or Diabetic Ketoacidosis (DKA).
- NEVER fill your tubing while your infusion set is connected to your body. Always ensure that the infusion set is disconnected from your body before changing the cartridge or filling the tubing. Failure to disconnect your infusion set from your body before changing the cartridge or filling the tubing can result in over delivery of insulin. This can cause hypoglycemia (low BG) events.
- DO NOT start to use your pump before reading the user guide. Failure to follow the instructions in this user guide can result in over delivery or under delivery of insulin. This can cause hypoglycemia (low BG) or hyperglycemia (high BG) events. If you have questions or need further clarification on your pump use, ask your healthcare provider or call your local customer support.
- DO NOT start to use your pump before you have been appropriately trained on its use by a certified trainer or through the training materials available online. Consult with your healthcare provider for your individual training needs for the pump. Failure to complete the necessary training on your pump could result in serious injury or death.
- ONLY use U-100 insulin analogs that have been tested and found to be compatible for use in the pump listed in the User Guide Section 1.7 Compatible Insulins. Only U-100 insulin analogs listed in Section 1.7 Compatible Insulins have been tested and found to be compatible for use in the pump. Use of insulin with greater or lesser

concentration can result in an over delivery or under delivery of insulin. This can cause hypoglycemia (low BG) or hyperglycemia (high BG) events.

- For patients whose insulin administration is managed by a caregiver, it is recommended to turn off the Quick Bolus feature to avoid inadvertent bolus delivery. Inadvertent Pump button presses could result in over delivery of insulin. This can cause hypoglycemia (low BG) events. However, if your smartphone is lost or damaged, you will NOT be able to deliver a bolus using your pump. Contact your healthcare provider for an alternate insulin delivery plan if your smartphone is not available and the Quick Bolus feature is not enabled.

***Note: refer to the User Guide for all warnings and precautions. The summary above lists the most relevant warnings based on risks to patients from the available evidence.**

4.2.2. Warnings & Precautions for Healthcare Professionals

Refer to summarized warnings and precautions listed above. For a full listing of warnings and precautions, refer to the User Guide.

4.3. Summary of Any Field Safety Corrective Actions

The following is a summary listing of field safety corrective actions for the Tandem Mobi Insulin Pump with Control-IQ+ Technology or the Tandem Mobi Mobile App. Also listed below are field actions related to the equivalent devices, the Tandem t:slim X2 insulin pump with Control-IQ/Control+ technology and the Tandem t:slim Mobile App.

4.3.1. Field Safety Corrective Actions – Tandem Mobi Insulin Pump with Control+ Technology

The following is a summary listing of field safety corrective actions for the Tandem Mobi Insulin Pump with Control-IQ+ technology:

Topic: CIQ+ Incorrect Interpolation
Field Action Type: Field Correction Notice
Geography(ies): USA
Initiation Date: 27-FEB-2025

Topic: Unexpected Automatic Correction Bolus
Field Action Type: Field Correction Notice
Geography(ies): USA
Initiation Date: 06-OCT-2025, follow up to field safety alert dated 05-AUG-2025

Topic: Malfunction 12, Vibe Motor
Field Action Type: Field Correction Notice
Geography(ies): USA
Initiation Date: 06-OCT-2025

4.3.2. Field Safety Corrective Actions – t:slim X2 Insulin Pump with Control-IQ/Control-IQ+ Technology

The following is a summary listing of field safety corrective actions for the t:slim X2 insulin pump with Control-IQ and Control-IQ+ technology:

Topic: Pump Age Reminder - Patients Younger Than 6 Years Old
Field Action Type: Field Safety Notice
Geography(ies): France
Initiation Date: 17-Jan-2022

Topic: Basal Rate Setting
Field Action Type: Field Safety Notice
Geography(ies): Global - Outside of the US
Initiation Date: 23-Feb-2022

Topic: X.6 Software Launch
Field Action Type: Field Correction Notice (U.S.), Field Safety Notice (OUS)
Geography(ies): Global
Initiation Date: 22-May-2022

Topic: Fill Tubing While Connected
Field Action Type: Field Safety Notice
Geography(ies): France
Initiation Date: 02-Dec-2024

Topic: CIQ+ Incorrect Interpolation
Field Action Type: Field Correction Notice
Geography(ies): USA
Initiation Date: 27-FEB-2025

Topic: Unexpected Automatic Correction Bolus
Field Action Type: Field Correction Notice
Geography(ies): USA
Initiation Date: 21-OCT-2025, follow up to field safety alert dated 05-AUG-2025

Topic: Malfunction 16, Potential Speaker Malfunction
Field Action Type: Field Safety Notice
Geography(ies): Multiple Countries
Initiation Date: 22-JUL-2025

4.3.3. Field Safety Corrective Actions – t:slim Mobile App

The following is a summary listing of field safety corrective actions for the Tandem t:slim Mobile App:

Topic: Mobile App Crashing Resulting in Pump Battery Depletion
Field Action Type: Field Correction Notice
Geography(ies): United States
Initiation Date: 26-Mar-2024

5. Summary of Clinical Evaluation and Post Market Clinical Follow-up

5.1. Summary of Clinical Data related to an Equivalent Device

The Tandem Mobi Insulin Pump with Control-IQ+ Technology and Tandem Mobi 2mL cartridge were evaluated based on data from the equivalent device, the t:slim X2 Insulin Pump with Control-IQ and Control-IQ+ technology, and t:slim 3mL cartridges, which were assessed based on prospective randomized clinical studies and single arm studies.

Table 1. Summary of The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas A Pivotal Study of t:slim X2 with Control-IQ Technology

Study	The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas A Pivotal Study of t:slim X2 with Control-IQ Technology (clinicaltrials.gov identifier: NCT03563313)
Subject Device	t:slim X2 insulin pump with Control-IQ technology, t:slim X2 3mL cartridge
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII).
Objective of Study	To assess efficacy and safety of the t:slim X2 insulin pump with Control-IQ technology in a large randomized controlled trial.
Study Design	Prospective, randomized, multicenter, study
Primary/Secondary Endpoints	Primary Efficacy Endpoint Time in target range of 70-180 mg/dL measured by CGM in CLC group vs. SAP group Secondary Efficacy Endpoints CGM-measured % time above 180 mg/dL CGM-measured mean glucose HbA1c at 26 weeks CGM-measured % time below 70 mg/dL CGM-measured % time below 54 mg/dL Other Secondary Efficacy Endpoints (considered exploratory): CGM Measured: % time in range 70-140 mg/dL Glucose variability measured with the coefficient of variation (CV) Glucose variability measured with the standard deviation (SD) % time < 60 mg/dL Low blood glucose index Hypoglycemia events (defined as at least 15 consecutive minutes < 70 mg/dL

	% time > 250 mg/dL % time > 300 mg/dL High blood glucose index HbA1c: HbA1c < 7.0% at 26 weeks HbA1c <7.5% at 26 weeks HbA1c improvement from baseline to 26 weeks > 0.5% HbA1c improvement from baseline to 26 weeks > 1.0% HbA1c relative improvement from baseline to 26 weeks > 10% HbA1c improvement from baseline to 26 week > 1.0% or HbA1c < 7.0% at 26 weeks Questionnaires Fear of Hypoglycemia Survey (HFS-II) – total score and subscales Hyperglycemia Avoidance Scale – total score and subscales Diabetes Distress Scale – total score and subscales Hyperglycemia Confidence Scale – total score Clarke Hypoglycemia Awareness Scores INSPIRE survey scores System Usability Scale (SUS)
Inclusion Criteria	1. Clinical diagnosis, based on investigator assessment of type 1 diabetes for at least 1-year and using insulin for at least 1-year 2. Familiarity and use of a carbohydrate ratio for meal boluses 3. Age ≥ 14 years old 4. For females, not currently known to be pregnant (*if female and sexually active, must agree to use a form of contraception to prevent pregnancy while a participant in the study. A negative serum or urine pregnancy test will be required for all females of child-bearing potential. Participants who become pregnant will be discontinued from the study. Also, participants who during the study develop and express the intention to become pregnant within the timespan of the study will be discontinued.* 5. For participants < 18 years old, living with one or more parent / legal guardian knowledgeable about emergency procedures for severe hypoglycemia and able to contact the subject in case of an emergency 6. Willingness to suspend use of any personal CGM for the duration of the clinical trial once the study CGM is in use 7. Willingness to use a regular insulin pump during the study with no automatic insulin adjustment based on glucose level when assigned to participate in an SAP group 8. Investigator has confidence that the participant can successfully operate all study devices and I capable of adhering to the protocol 9. Willingness to switch to lispro (Humalog) or aspart (Novolog) if not using already, and to use no other insulin besides lispro (Humalog) or aspart (Novolog) during the study. 10. Total daily insulin does (TDD) at least 10 U/day 11. Willingness not to start any new non-insulin glucose-lowering agent during the course of the trial.
Exclusion Criteria	1. Concurrent use of any non-insulin glucose-lowering agent other than metformin (including GLP-1 agonists, Symlin, DPP-4 inhibitors, SGLT-2 inhibitors, sulfonylureas)

<table>
<tr><td></td><td>2. Hemophilia or any other bleeding disorder
3. A condition which in the opinion of the investigatory or designee, would put the participant or study at risk
4. Participation in another pharmaceutical or device trial at the time of enrollment or during the study
5. Employed by, or having immediate family members employed by Tandem Diabetes Care, Inc. or TypeZero Technologies, LLC, or having a direct supervisor at place of employment who is also directly involved in conducting the clinical trial (as a study investigator, coordinator, etc.); or having a first-degree relative who is directly involved in conducting the clinical trial.</td></tr>
<tr><td>Number of Enrolled Subjects</td><td>Enrollment of 170 total subjects with randomization of 168 subjects.</td></tr>
<tr><td>Study Population</td><td>Women comprised 50% of the subjects. The age range was 14 to 71 years with the average age of 33 years.</td></tr>
<tr><td>Study Methods</td><td>Randomized clinical study with 2:1 randomization to intervention with the t:slim X2 insulin pump with Control-IQ technology vs. sensor augmented pump for 6 months.</td></tr>
<tr><td>Clinical Benefits</td><td>Use of the t:slim X2 insulin pump with Control-IQ technology was found to be safe and effective, increasing time in target range, reducing both hyperglycemia and hypoglycemia, and simultaneously improving glycated hemoglobin over a 26-week period.</td></tr>
<tr><td>Undesirable Side-Effects or Adverse Events</td><td>
<table>
<tr><th></th><th>Pre-randomization</th><th colspan="2">Post-randomization</th></tr>
<tr><th></th><th></th><th>CLC</th><th>SAP</th></tr>
<tr><td>Hyperglycemia with Ketosis</td><td>1</td><td>12</td><td>2</td></tr>
<tr><td>Diabetic Ketoacidosis (DKA)</td><td>-</td><td>1</td><td>-</td></tr>
<tr><td>Hyperglycemia without Ketosis</td><td>-</td><td>1</td><td>-</td></tr>
<tr><td>Concussion</td><td>-</td><td>1</td><td>-</td></tr>
<tr><td>Otitis Externa</td><td>-</td><td>1</td><td>-</td></tr>
<tr><td>Bypass Surgery</td><td>-</td><td>1</td><td>-</td></tr>
<tr><td>Total</td><td>1</td><td>17</td><td>2</td></tr>
</table>
</td></tr>
<tr><td>Long-term Benefits and Risk</td><td>Long-term benefits and risk were not assessed as part of this study.</td></tr>
<tr><td>Limitations of Study</td><td>There were more unscheduled contacts in the closed-loop group, which was attributed to the use of an investigational device, and the insulin pumps used by the control group did not have a feature to suspend insulin for predicted hypoglycemia, which is now available for some pumps and has been shown to reduce the amount of continuous glucose monitor–measured hypoglycemia.</td></tr>
</table>

Device Deficiency or Device Replacements due to Safety and/or Performance				
	CLC Treatment Group		SAP Treatment Group	
	Control-IQ	Dexcom G6	SAP Pump	Dexcom G6
Connectivity Problem	82	2	-	-
Component failure requiring replacement	17	9	1	1
Inappropriate error message/alert	28	4	-	1
Component failure requiring reset/reboot	6	-	-	-
Inappropriate calibration related behavior	1	2	-	-
Frozen/unresponsive interface	2	-	-	-
Unknow error message / alert	1	-	-	-
Total	137	17	1	2

Table 2. Summary of The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas, Extension Phase A Pivotal Study of t:slim X2 with Control-IQ Technology

Study	The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas, Extension Phase A Pivotal Study of t:slim X2 with Control-IQ Technology (clinicaltrials.gov identifier: NCT03563313)
Subject Device	t:slim X2 insulin pump with Control-IQ technology, t:slim X2 3mL cartridge
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL Cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII).
Objective of Study	1) Among subjects who used Control-IQ in the original RCT, to compare continued use of Control-IQ for 3 months versus switching to Basal-IQ (PLGS) for 3 months, and 2) Among subjects who used SAP in the original RCT, to obtain additional safety data by initiating use of Control-IQ in an observational study for 3 months.
Study Design	Prospective, single arm, multicenter, study

Primary/Secondary Endpoints	Primary Efficacy Endpoint time in target range of 70-180 mg/dL measured by CGM in CLC group vs. PLGS group over 3 months. For the observational study in subjects who used SAP during the original RCT, then switched to Control-IQ for 3 months, safety outcomes are primary. Additional Outcome Measures CGM Measured: Overall control and Hyperglycemia % time in range 70-180 mg/dL % time > 180 mg/dL Mean glucose % time > 250 mg/dL % time > 300 mg/dL High blood glucose index % time in range 70-140 mg/dL Hypoglycemia % <70 mg/dL % <54 mg/dL % <60 mg/dL Low blood glucose index Hypoglycemia events (defined as at least 15 consecutive minutes <70 mg/dL) Glucose Variability Coefficient of variation (CV) Standard deviation HbA1c: HbA1c at 13 weeks HbA1c < 7.0% at 13 weeks HbA1c <7.5% at 13 weeks HbA1c improvement from baseline to 13 weeks > 0.5% HbA1c improvement from baseline to 13 weeks > 1.0% HbA1c relative improvement from baseline to 13 weeks > 10% HbA1c improvement from baseline to 13 weeks > 1.0% or HbA1c < 7.0% at 13 weeks Other Endpoints Questionnaires Fear of Hypoglycemia Survey (HFS-II) – total score subscales Hyperglycemia Avoidance Scale – total score and subscales Diabetes Distress Scale – total score and subscales Hyperglycemia Confidence Scale – total score Clarke Hypoglycemia Awareness Scores INSPIRE survey scores System Usability Scale (SUS) Technology Acceptance Survey Control-IQ Patient-Report Outcomes Questionnaire
Inclusion Criteria	1. Successful completion of the original 6-month RCT within the prior 14 days. 2. For females, not currently known to be pregnant. If female and sexually active, subjects agreed to use a form of contraception to prevent pregnancy while a participant in the study. A negative urine pregnancy test was required for all females of child-bearing potential. Participants who

	became pregnant were discontinued from the study (no subjects became pregnant during the study). 3. For participants <18 years old, living with one or more parent/legal guardian knowledgeable about emergency procedures for severe hypoglycemia and able to contact the participant in case of an emergency was required. 4. Willingness to not use a personal CGM for the duration of the study. 5. Investigator had confidence that the participant could successfully operate all study devices and was capable of adhering to the protocol. 6. Willingness to use only Lispro (Humalog) or Aspart (Novolog), and to use no other insulin during the study. 7. Willingness not to start any new non-insulin glucose-lowering agent during the course of the trial
Exclusion Criteria	1. Failure to have successfully completed the original 6-month RCT within the previous 14 days 2. Concurrent use of any non-insulin glucose-lowering agent other than metformin (including GLP-1 agonists, Symlin, DPP-4 inhibitors, SGLT-2 inhibitors, sulfonylureas) 3. Hemophilia or any other bleeding disorder 4. A condition which in the opinion of the investigatory or designee, would put the participant or study at risk 5. Participation in another pharmaceutical or device trial at the time of enrollment or during the study 6. Employed by, or having immediate family members employed by Tandem Diabetes Care, Inc. or TypeZero Technologies, LLC, or having a direct supervisor at place of employment who is also directly involved in conducting the clinical trial (as a study investigator, coordinator, etc.); or having a first-degree relative who is directly involved in conducting the clinical trial.
Number of Enrolled Subjects	164 subjects
Study Population	Age (Mean ± SD): 33 ± 16 years Gender (% female): 50% female
Study Methods	A 13-week extension study for subjects who completed the preceding 6 month randomized controlled trial (RCT; DCLP3) of Control-IQ vs. sensor-augmented pump (SAP). Subjects in the original RCT sensor-augmented pump (SAP) Group used Control-IQ during the extension study. Subjects in the original RCT Control-IQ Group were randomly assigned 1:1 to either continue Control-IQ or switch to Basal-IQ (Tandem predictive low-glucose suspend—PLGS—system).
Clinical Benefits	Use of the t:slim X2 insulin pump with Control-IQ technology was found to be safe and effective during the original 6-month RCT and provided sustained results throughout the 13-week extension study.

Undesirable Side-Effects or Adverse Events

	CLC-CLC N=54	CLC-PLGS N=55	SAP-CLC N=55
Severe Hypoglycemia Events	0	0	0
Diabetic Ketoacidosis Events	0	0	0
Serious Adverse Events Related to the Study Device	0	0	0
Other Serious Adverse Events	0	0	0
Hyperglycemia/Ketosis Events without DKA	0	3	2
Total	**0**	**3**	**2**

Long-term Benefits and Risk

Long-term benefits and risk were not assessed as part of this study.

Limitations of Study

No limitations for this study were reported

Device Deficiency or Device Replacements due to Safety and/or Performance

	CLC-CLC Treatment Group		CLC-PLGS Treatment Group			CLC-CLC Treatment Group	
	Control-IQ	Dexcom G6	Basal-IQ	Dexcom G6	Other	Control-IQ	Dexcom G6
Connectivity Problem			1				
Component failure requiring replacement	2	1	9	2		1	3
Infusion set failure			1		1	1	
Component failure requiring reset/reboot	1		10			3	
Unexpected Battery Depletion						1	
Frozen/unresponsive interface			1				
Malfunction requiring software patch	1					1	
User Error						1	
Total	137	17	1	2			

Table 3. Summary of The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas in Pediatrics A Study of t:slim X2 with Control-IQ Technology

Study	The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas in Pediatrics - A Study of t:slim X2 with Control-IQ Technology (clinicaltrials.gov identifier: NCT03844789)
Subject Device	t:slim X2 insulin pump with Control-IQ technology, t:slim X2 3mL cartridge
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII).
Objective of Study	To assess efficacy and safety of the t:slim X2 insulin pump with Control-IQ technology in a randomized controlled trial.
Study Design	Prospective, randomized, multicenter, study
Primary/Secondary Endpoints	Primary Efficacy Endpoint CGM-measured % in range 70-180 mg/dL Secondary Efficacy Endpoints CGM-measured % above 180 mg/dL CGM-measured mean glucose HbA1c at 16 weeks CGM-measured % below 70 mg/dL CGM-measured % below 54 mg/dL CGM-measured % above 250 mg/dL Glucose variability measured with the coefficient of variation (CV) Other Secondar Efficacy Endpoints CGM-Measured % in range 70-140 mg/dL glucose variability measured with the standard deviation (SD) % <60 mg/dL low blood glucose index hypoglycemia events (defined as at least 15 consecutive minutes <70 mg/dL) % >300 mg/dL high blood glucose index % in range 70-180 mg/dL improvement from baseline to 16 weeks ≥5% % in range 70-180 mg/dL improvement from baseline to 16 weeks ≥10% HBA1c HbA1c <7.5% at 16 weeks 1469 HbA1c improvement from baseline to 16 weeks >0.5% 1470 HbA1c improvement from baseline to 16 weeks >1.0% 1471

	HbA1c relative improvement from baseline to 16 weeks >10% 1472 HbA1c improvement from baseline to 16 weeks >1.0% or HbA1c <7.0% at 16 weeks Questionnaires Fear of Hypoglycemia Survey (HFS-II) total score and subscales Clarke Hypoglycemia Awareness Scores Problem Areas In Diabetes Survey (PAID) INSPIRE survey scores PedsQL Diabetes Module total score and subscales Pittsburgh Sleep Quality Index (Parent only) System Usability Scale (SUS) Other: Total daily insulin (units/kg) Basal: bolus insulin ratio Weight and Body Mass Index (BMI)
Inclusion Criteria	1. Clinical diagnosis, based on investigator assessment, of type 1 diabetes for at least 1-year and using insulin for at least 1-year 2. Familiarity and use of a carbohydrate ratio for meal boluses 3. Age ≥ 6 and ≤ 13 years old 4. Weight ≥ 25 kg and ≤ 140 kg 5. For females, not currently known to be pregnant (if female and sexually active, must agree to use a form of contraception to prevent pregnancy while a participant in the study. A negative serum or urine pregnancy test was required for all females of child-bearing potential. Participants who become pregnant would have been discontinued from the study. Also, participants who during the study develop and express the intention to become pregnant within the timespan of the study would have been discontinued. 6. Living with at least one parent or guardian who was knowledgeable about emergency procedures for severe hypoglycemia (and was able to contact emergency services and study staff) 7. Willingness to suspend use of any personal closed-loop system (except t:slim X2 insulin pump with Basal-IQ if in the control group) that they use at home for the duration of the clinical trial once the study CGM is in use 8. Investigator has confidence that the participant (or parent/guardian) can successfully operate all study devices and is capable of adhering to the protocol 9. Willingness to switch to lispro (Humalog) or aspart (Novolog) if not using already, and to use no other insulin besides lispro (Humalog) or aspart (Novolog) during the study. This includes: a. Participants randomized to Control-IQ technology b. Participants on MDI treatment, randomized to the SAP group that will be provided a t:slim X2 insulin pump to use during the study 10. Total daily insulin dose (TDD) of at least 10 U/day 11. Willingness not to start any new non-insulin glucose-lowering agent during the course of the trial. 12. Participant and parent(s)/guardian(s) willingness to participate in all training sessions as directed by study staff.

<table>
<tr><td>Exclusion Criteria</td><td>1. Concurrent use of any non-insulin glucose-lowering agent other than metformin (including GLP-1 agonists, Symlin, DPP-4 inhibitors, SGLT-2 inhibitors, sulfonylureas)
2. Hemophilia or any other bleeding disorder
3. A condition which in the opinion of the investigatory or designee, would put the participant or study at risk
4. Participation in another pharmaceutical or device trial at the time of enrollment or during the study
5. Employed by, or having immediate family members employed by Tandem Diabetes Care, Inc. or TypeZero Technologies, LLC, or having a direct supervisor at place of employment who is also directly involved in conducting the clinical trial (as a study investigator, coordinator, etc.); or having a first-degree relative who is directly involved in conducting the clinical trial.</td></tr>
<tr><td>Number of Enrolled Subjects</td><td>101 subjects</td></tr>
<tr><td>Study Population</td><td>All 101 subjects were between the ages of 6 and 13 years with the median age of 11 years in the CLC group and 10 years in the SAP group. Thirty-eight percent of the subjects were female.</td></tr>
<tr><td>Study Methods</td><td>Eligible participants not currently using an insulin pump and Dexcom CGM with minimum data requirements will initiate a run-in phase of 2-4 weeks that will be customized based on whether the participant is already a pump or CGM user. Participants who skip or successfully complete the run-in will be randomly assigned 3:1 to the use of closed-loop control (CLC group) using t:slim X2 insulin pump with Control-IQ Technology vs. Control Group for 16 weeks. The Control Group will be offered to transition to use CLC and the experimental arm will extend their use of CLC for 12 weeks.</td></tr>
<tr><td>Clinical Benefits</td><td>Use of the t:slim X2 insulin pump with Control-IQ technology was found to be safe and effective, increasing time in target range and reducing hyperglycemia over a 16-week period.</td></tr>
<tr><td>Undesirable Side-Effects or Adverse Events</td><td>
<table>
<tr><th></th><th colspan="2"># Events / # of Participants</th></tr>
<tr><th></th><th>CLC (N=78)</th><th>SAP (=23)</th></tr>
<tr><td>Adverse Event Related to the Study Device</td><td>13/13</td><td>2/1</td></tr>
<tr><td>Abscess at Sensor Site</td><td>0/0</td><td>2/1</td></tr>
<tr><td>Hyperglycemia</td><td>2/2</td><td>0/0</td></tr>
<tr><td>Ketosis</td><td>10/10</td><td>0/0</td></tr>
<tr><td>Accidental over-delivery of Insulin</td><td>1/1</td><td>0/0</td></tr>
<tr><td>Adverse Events Not Related to the Study Device</td><td>3/2</td><td>1/1</td></tr>
<tr><td>Hypoglycemia</td><td>1/1</td><td>0/1</td></tr>
<tr><td>Ketosis</td><td>2/2</td><td>1/1</td></tr>
</table>
</td></tr>
<tr><td>Long-term Benefits and Risk</td><td>Long-term benefits and risk were not assessed as part of this study.</td></tr>
<tr><td>Limitations of Study</td><td>Although eligibility criteria were broad, the trial population was not fully representative of the general population with respect to socioeconomic status,</td></tr>
</table>

	glycated hemoglobin levels, and the use of devices (pumps and continuous glucose monitors) in diabetes management.
Device Deficiency or Device Replacements due to Safety and/or Performance	

	Pre-randomization	Post-randomization	
		CL	SAP
Component failure requiring replacement	2	19	2
User Error	1	6	0
Connectivity Problem	0	2	0
Device-related AE	0	0	2
Component failure requiring reset/reboot	0	1	0
Unknown Error Message	0	1	0
Total	**3**	**29**	**4**

Table 4. Summary of The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas in Pediatrics – Extension Study A Study of t:slim X2 with Control-IQ Technology

Study	The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas in Pediatrics – Extension Study A Study of t:slim X2 with Control-IQ Technology (clinicaltrials.gov identifier: NCT03844789)
Subject Device	t:slim X2 insulin pump with Control-IQ technology, t:slim X2 3mL cartridge
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII).
Objective of Study	To assess the sustained efficacy and safety of the t:slim X2 insulin pump with Control-IQ technology)in pediatrics, during the Extension Study of the RCT in which all participants used the system for an additional 12 weeks.
Study Design	Prospective, single arm, multicenter study
Primary/Secondary Endpoints	The primary endpoint for this extension study was the improvement in time in target range (70-180 mg/dL) measured by CGM in the SAP group after transitioning to the t:slim X2 insulin pump Control-IQ technology for the 12-week extension study, compared with the same group during the main RCT phase. The following exploratory endpoints were also reported:

	CGM-Measured % Time in range 70-180 mg/dL % Time in range 70-140 mg/dL Mean glucose Glucose variability measured with the standard deviation (SD) Glucose variability measured with the coefficient of variation (CV) % Time above 180 mg/dL % Time >250 mg/dL % Time >300 mg/dL o High blood glucose index % Time <70 mg/dL % Time <60 mg/dL % Time <54 mg/dL Low blood glucose index (LBGI) Hypoglycemia events (defined as at least 15 consecutive minutes <70 mg/dL) % in range 70-180 mg/dL improvement from 16-week baseline to 28 weeks ≥5% % in range 70-180 mg/dL improvement from 16-week baseline to 28 weeks ≥10% HBA1c HbA1c at 28 weeks HbA1c < 7.0% at 28 weeks HbA1c <7.5% at 28 weeks HbA1c improvement from 16-week baseline to 28 weeks > 0.5% HbA1c improvement from 16-week baseline to 28 weeks > 1.0% HbA1c relative improvement from 16-week baseline to 28 weeks > 10% HbA1c improvement from 16-week baseline to 28 weeks > 1.0% or HbA1c < 7.0% at 28 weeks Questionnaires Fear of Hypoglycemia Survey (HFS-II) total score, Behavior (avoidance and maintain high BG) and Worry (helplessness and social consequences) scores Clarke Hypoglycemia Awareness Scores Problem Areas in Diabetes Survey (PAID) INSPIRE survey scores Pediatric Quality of Life Diabetes Module – total score and 5 subscales: Diabetes Treatment I Treatment II Worry Communication Pittsburgh Sleep Quality Index (Parent only) System Usability Scale (SUS)
Inclusion Criteria	Successful completion of the 4-month DCLP5 RCT
Exclusion Criteria	Failure to complete the 4-month DCLP5 RCT
Number of Enrolled Subjects	100 subjects
Study Population	All 100 subjects were between the ages of 6 and 13 years with the mean age of 11 years in the CLC-CLC group and 10 years in the SAP-CLC group. Female subjects comprised 49% and 50% of the two treatment groups, respectively.

<table>
<tr><td>Study Methods</td><td>This is the Extension Study of the DCLP5 Randomized Clinical Trial, which was a planned extension included in the approved IDE protocol. After the first phase (4 month parallel group RCT with 3:1 randomization to intervention with the closed loop system (CLC) vs. sensor-augmented pump (SAP)), the Extension Study consisted of the subsequent 12 weeks in which the original control group used the closed loop system (SAP-CLC) and the original intervention group extended the use of the closed loop system for the same period (CLC-CLC).</td></tr>
<tr><td>Clinical Benefits</td><td>Use of t:slim X2 insulin pump with Control-IQ technology was found to be safe and effective, increasing time in target range and reducing hyperglycemia; improvements that were apparent from the first day of use and sustained throughout a 28-week period.</td></tr>
<tr><td>Undesirable Side-Effects or Adverse Events</td><td>
<table>
<tr><th></th><th colspan="2"># Events / # of Participants</th></tr>
<tr><th></th><th>CLC-CLC (N=78)</th><th>SAP-CLC (=22)</th></tr>
<tr><td>Adverse Event Related to the Study Device</td><td>7/6</td><td>2/1</td></tr>
<tr><td>Hyperglycemia with or without ketosis due to pump infusion set problem</td><td>6/5</td><td>2/1</td></tr>
<tr><td>Hyperglycemia with or without ketosis due to CGM problem</td><td>1/1</td><td>0/0</td></tr>
<tr><td>Adverse Events Not Related to the Study Device</td><td>0/0</td><td>1/1</td></tr>
<tr><td>Ketosis due to illness</td><td>0/0</td><td>1/1</td></tr>
</table>
</td></tr>
<tr><td>Long-term Benefits and Risk</td><td>Long-term benefits and risk were not assessed as part of this study.</td></tr>
<tr><td>Limitations of Study</td><td>Although eligibility criteria were broad, the trial population was not fully representative of the general population with respect to socioeconomic status, glycated hemoglobin levels, and the use of devices (pumps and continuous glucose monitors) in diabetes management.</td></tr>
<tr><td>Device Deficiency or Device Replacements due to Safety and/or Performance</td><td>See below for types of device issues in the extension study by treatment group:
<table>
<tr><th></th><th>CLC-CLC</th><th>SAP-CLC</th></tr>
<tr><td>Component failure requiring replacement</td><td>14</td><td>3</td></tr>
<tr><td>User Error</td><td>1</td><td>0</td></tr>
<tr><td>Unknown Error Message</td><td>2</td><td>2</td></tr>
<tr><td>Total</td><td>17</td><td>5</td></tr>
</table>
</td></tr>
</table>

Table 5. Summary of The Pediatric Artificial Pancreas (PEDAP) trial: A Randomized Controlled Comparison of the Control-IQ technology Versus Standard of Care in Young Children in Type 1 Diabetes

Study	The Pediatric Artificial Pancreas (PEDAP) trial: A Randomized Controlled Comparison of the Control-IQ technology Versus Standard of Care in Young Children in Type 1 Diabetes (clinicaltrials.gov identifier: NCT04796779)
Subject Device	t:slim X2 insulin pump with Control-IQ technology, t:slim X2 3mL cartridge
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII).
Objective of Study	To assess efficacy, quality of life, and safety of a closed loop control (CLC) system (t:slim X2 insulin pump with Control-IQ technology) in a randomized controlled trial in children 2 to <6 years old with type 1 diabetes compared to standard care (SC)
Study Design	Multisite, randomized controlled clinical trial
Primary/Secondary Endpoints	The primary efficacy endpoint was CGM-measured % in range 70–180 mg/dL between Control-IQ (Closed-Loop Control, CLC) and standard care (SC) - defined as either multiple daily injections of insulin (MDI) or use of an insulin pump without HCL capabilities (low-glucose suspend or predictive low-glucose suspend functionality was permitted) in conjunction with study CGM over 13 weeks. The following secondary endpoints were tested in a hierarchical fashion to preserve the overall type 1 error: • CGM-measured % above 250 mg/dL • CGM-measured mean glucose • HbA1c at 13 weeks • CGM-measured % below 70 mg/dL • CGM-measured % below 54 mg/dL Exploratory efficacy endpoints included various CGM-based measures of glycemic control and binary HbA1c assessments. Other key outcomes included a set of psychosocial questionnaires, insulin delivery metrics, and measures of weight and Body Mass Index (BMI).
Inclusion Criteria	The study cohort included children 2 to <6 years old with type 1 diabetes (T1D) for at least 6 months and using insulin for at least 6 months.

	Participants' total daily insulin dose had to be at least 5 U/day, with body weight at least 20 lbs.
Exclusion Criteria	Exclusions included use of any non-insulin glucose-lowering agent; hemophilia or any other bleeding disorder; >1 severe hypoglycemic event with seizure or loss of consciousness in the last 3 months; >1 DKA event in the last 6 months not related to illness, infusion set failure, or initial diagnosis; history of chronic renal disease or currently on hemodialysis; history of adrenal insufficiency; hypothyroidism that was not adequately treated; any other condition, which in the opinion of the investigator or designee, would put the participant or study at risk; and current use of a hybrid closed-loop (HCL) system.
Number of Enrolled Subjects	102 subjects
Study Population	Mean age was 3.84±1.23 years (Range 2.00–5.98) in CLC group, and 4.06±1.25 year (Range 2.02–5.90) in the SC group.
Study Methods	After consent was signed, eligibility was assessed. Eligible participants not currently using a Dexcom G5 or Dexcom G6 continuous glucose monitor (CGM) meeting minimum usage requirements initiated a run-in phase of 2 to 6 weeks that was customized based on whether the participant was already a CGM user. Participants who skipped or successfully completed the run-in were randomly assigned 2:1 to an intervention using Tandem t:slim X2 with Control-IQ Technology or the standard care (SC) control group using existing insulin therapy in conjunction with study CGM. A phone or videoconference contact occurred 3 (±2) days after randomization only for participants on MDI at enrollment assigned to the CLC group. Additional phone/videoconference contacts occurred at 7 (±2) days and 10 weeks (±7 days) after randomization. Visits occurred at 2 weeks (±4 days), 6 weeks (±7 days), and 13 weeks (±7 days) after randomization. Most visits were conducted virtually. At randomization and at the 13-week visit, a blood sample was obtained for central lab HbA1c determination. At screening and at the 13-week visit, psychosocial questionnaires were completed.
Clinical Benefits	During this randomized, controlled trial, participants using CLC had significantly higher time in the target range of 70 to 180 mg/dL, an approximately 3 hours per day increase, compared with participants in the SC group who used CGM in conjunction with their usual insulin delivery method. The benefit in increasing time in target range was observed across the spectrum of participant characteristics including age, race-ethnicity, parental education, family income, baseline glycated hemoglobin level, and pre-study insulin delivery method (insulin pump or insulin injections). The beneficial effect of CLC was also reflected in reductions in time >250 mg/dL, mean glucose, and glycated hemoglobin levels. The amount of CGM-measured hypoglycemia was low at baseline and did not differ between groups in follow up.

	Participants used the CLC system safely. The frequency of clinical severe hypoglycemia events and CGM-measured hypoglycemia events were low and similar in the two groups. More occurrences of pump infusion site failure leading to hyperglycemia with or without ketosis were reported in the CLC group compared with the SC group. However, this likely reflects differential reporting between groups, as noted in other studies. This presumption is supported by the finding of a lower rate of prolonged hyperglycemia events in the CLC group compared with the SC group. The study was conducted during the public health emergency due to COVID-19 in the United States, which necessitated developing processes to train the participants' families on use of the CLC system virtually rather than the conventional approach with in-person visits. As a result, over 80% of CLC training and over 90% of all visits were conducted virtually. Successful use of CLC under these conditions is an important finding that could impact the approach to initiating and monitoring CLC system use and expand use of such systems, particularly for participants living in areas without an endocrinologist. In summary, in this 13-week trial involving children 2 to <6 years of age who had T1D with virtual device training for over 80% of participants, use of a hybrid closed-loop system with Control IQ Technology was safe and associated with an increase in glucose levels in target range compared with standard care insulin delivery used with CGM.
Undesirable Side-Effects or Adverse Events	Seventy-one adverse events were reported for 41 (60%) participants in the CLC group and 14 events for 11 (32%) participants in the SC group (P=0.001). There were two cases of severe hypoglycemia in the CLC group and one case in the SC group. One case of diabetic ketoacidosis occurred in the CLC group and none in the SC group.
Long-term Benefits and Risk	Long-term benefits and risk were not assessed as part of this study.
Limitations of Study	Overrepresentation of families with higher socioeconomic status in the trial cohort may affect the generalizability of the results. An additional limitation was the trial period of only 13 weeks. There were more contacts with the patients in the closed-loop group than with those in the stan- dard-care group; this is an inherent issue in trials in which one group is using an investiga- tional device and the other group is receiving standard care.
Device Deficiency or Device Replacements due to Safety and/or Performance	There were 51 reported hyperglycemia/ketosis events in the CLC group, mostly related to infusion set failures, and 8 in the SC group.

Table 6. Summary of The Pediatric Artificial Pancreas (PEDAP) trial: A Randomized Controlled Comparison of the Control-IQ technology Versus Standard of Care in Young Children in Type 1 Diabetes (Extension Phase)

Study	The Pediatric Artificial Pancreas (PEDAP) trial: A Randomized Controlled Comparison of the Control-IQ technology Versus Standard of Care in Young

	Children in Type 1 Diabetes (Extension Phase) (clinicaltrials.gov identifier: NCT04796779)
Subject Device	t:slim X2 insulin pump with Control-IQ+ technology, t:slim X2 3mL cartridge
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ+ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII).
Objective of Study	To assess efficacy, quality of life, and safety of a closed loop control (CLC) system (t:slim X2 with Control-IQ Technology) in an extension phase following a randomized controlled trial in children age 2 to <6 years old
Study Design	Extension phase following randomized trial in children 2 to <6 years old with type 1 diabetes

Primary/Secondary Endpoints	The Extension Phase reported below was preceded by a 13-week parallel group randomized controlled trial (RCT) comparing a Standard Care (SC) group (study CGM plus either multiple daily injections of insulin [MDI] or an insulin pump without hybrid closed-loop control) with a Closed-Loop Control (CLC) group (t:slim X2 with Control-IQ Technology).
	
	During the initial Extension Phase period (study weeks 14 to 26), the RCT SC group transitioned to use CLC for 13 weeks (SC-CLC) and the RCT CLC group continued use of CLC for the same period (CLC-CLC).
	
	Formal statistical comparisons between the RCT and Extension Phase were performed for key outcome measures including:
	• CGM-measured % in range 70-180 mg/dL (TIR)
	• CGM-measured % above 250 mg/dL
	• CGM-measured mean glucose
	• HbA1c at 13 weeks
	• CGM-measured % below 70 mg/dL
	• CGM-measured % below 54 mg/dL
	• PedsQL Diabetes Module – total score
	• Pediatric Inventory for Parents (PIP)
	  ○ Frequency domain total score
	  ○ Difficulty domain total score
	• INSPIRE Survey
	• Pittsburgh Sleep Quality Index (PSQI) global score
	• Fear of Hypoglycemia Survey for Parents (HFS-P) – total score
	• Hypoglycemia Confidence Scale (HCS)
	• System Usability Scale (SUS)

	Safety outcomes included the following:
	• Number of severe hypoglycemia (SH) events and SH event rate per 100 person-years
	• Number of DKA events and DKA event rate per 100 person-years
	• Other serious adverse events
	• Any reportable adverse event
	• Number of calendar days with any ketone level ≥1.0 mmol/L
	• Investigational device related:
	  ○ Adverse device effects (ADE)
	  ○ Serious adverse device events (SADE)
	  ○ Unanticipated adverse device effects (UADE)
	Other outcomes included insulin delivery metrics and measures of weight and Body Mass Index (BMI).
	For the Extended Use period (beyond Week 26), outcomes were analogous to those calculated for the initial Extension Phase period.
	Challenge period outcomes included safety events and CGM metrics during the challenge period, and up to 4 hours after the challenge period, and overnight after the challenges.

Inclusion Criteria	Participants in the preceding RCT were children 2 to <6 years old with type 1 diabetes (T1D) treated with insulin for at least 6 months. Participants' total daily insulin dose had to be at least 5 U/day, with body weight at least 20 lbs.
Exclusion Criteria	Exclusions included use of any non-insulin glucose-lowering agent; hemophilia or any other bleeding disorder; >1 severe hypoglycemic event with seizure or loss of consciousness in the last 3 months; >1 diabetic ketoacidosis event (D/A) event in the last 6 months not related to illness, infusion set failure, or initial diagnosis; history of chronic renal disease or currently on hemodialysis; history of adrenal insufficiency; hypothyroidism that was not adequately treated; any other condition, which in the opinion of the investigator or designee, would put the participant or study at risk; and current use of a hybrid closed-loop (HCL) system.
Number of Enrolled Subjects	96 subjects
Study Population	Mean age was 4.10±1.23 years (Range 2.30–6.33) in the CLC-CLC group, and 4.32±1.23 years (Range 2.35–6.22) in the SC-CLC group.
Study Methods	The Extension Phase reported below was preceded by a 13-week parallel group randomized controlled trial (RCT) comparing a Standard Care (SC) group (study CGM plus either multiple daily injections of insulin [MDI] or an insulin pump without hybrid closed-loop control) with a Closed-Loop Control (CLC) group (t:slim X2 with Control-IQ Technology). During the initial Extension Phase period (study weeks 14 to 26), the RCT SC group transitioned to use CLC for 13 weeks (SC-CLC) and the RCT CLC group continued use of CLC for the same period (CLC-CLC). After the 26-week visit, participants could continue using CLC for an additional Extended Use period that ended on July 31, 2022. A subset of participants participated in an optional exercise/meal challenge

	ancillary study, which included 1) a skipped meal bolus, 2) a full meal bolus plus exercise, and 3) a separate exercise session. An updated version (1.5) of the Control-IQ system with enhanced usability and specific algorithm changes designed to improve safety and performance for this population of low insulin users (low total daily dose) was used during the Extension Phase and Extended Use periods. Participants assigned to the RCT SC group received full training based on the updated pump, while participants assigned to the RCT CLC group received a brief training session to review any new or changed features of the pump. A phone or videoconference contact occurred 3 (±2) days after Extension Phase initiation. Additional phone contacts occurred at 14 weeks (±2 days) and 23 weeks (±7 days). Additional videoconferences or clinic visits occurred at 15 weeks (±4 days), 19 weeks (±7 days), and 26 weeks (±7 days). During the Extended Use period that began at Week 26, participants had videoconferences or clinic visits every 13 weeks (±7 days) until the end of the study. Most visits were conducted virtually. At the 26-week visit, a blood sample was obtained for central lab HbA1c determination, psychosocial questionnaires were completed, and a subset of participants took part in a Focus Group session. At each successive 13-week interval during the Extended Use period, another blood sample was obtained for central lab HbA1c determination.
Clinical Benefits	In this 13-week Extension Phase plus Extended Use period following completion of the PEDAP RCT involving children 2 to <6 years of age with T1D, use of a hybrid closed-loop system with Control-IQ+ technology was safe and effective over a sustained period of time, comprising a total system use combining the RCT, Extension Phase, and Extended Use period of 23,582 days (64.6 participant-years). Results also showed that the use of the t:slim X2 insulin pump with Control-IQ+ technology in this young age group is associated with robust improvements in commonly used PROs, and user experience interviews highlight benefits beyond glycemic outcomes.
Undesirable Side-Effects or Adverse Events	In both the CLC-CLC group and SC-CLC group, there were few serious adverse events. Two severe hypoglycemia events occurred, unrelated to the study device. There were no DKA events. During meal and exercise challenges, there were no serious adverse events or study-related adverse events and CGM metrics showed no concerns either during the challenges, immediately after the challenges, or overnight after the challenges.
Long-term Benefits and Risk	Long-term benefits and risk were not assessed as part of this study.
Limitations of Study	Less than one- third of participants completed user experience interviews. It is possible the experiences provided by those who participated do not fully reflect the entire sample.
Device Deficiency or Device Replacements due	Hyperglycemia with or without ketosis due to either infusion set failure or illness were frequent and not unexpected. There were no unanticipated adverse device effects.

to Safety and/or Performance	

Table 7. Summary of Control-IQ Technology for High Insulin Users (Higher-IQ)

Study	Control-IQ Technology for High Insulin Users with Type 1 Diabetes (Higher-IQ) (clinicaltrials.gov identifier: NCT05422053)
Subject Device	t:slim X2 insulin pump with Control-IQ+ technology, t:slim X2 3mL cartridge
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ+ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII).
Objective of Study	To assess the safety and explore glycemic outcomes with use of an AID system (t:slim X2 insulin pump with Control-IQ+ Technology) in adults with type 1 diabetes (T1D) who planned to use at least one basal rate > 3 units/hour
Study Design	Single-arm, multi-center, prospective clinical study for 13 weeks.
Primary/Secondary Endpoints	Primary Safety Endpoints: • Severe hypoglycemia (with cognitive impairment such that assistance of another individual is needed for treatment) during study compared with data on severe hypoglycemic events reported by T1D Exchange clinic registry over a three-month time period • Diabetic ketoacidosis (event rate) • Number of unanticipated adverse device effects (UADEs) • Number of other serious adverse events (SAEs) Secondary Safety Endpoints: • All adverse events • CGM hypoglycemia outcomes ◆ Overall % time <54 mg/dL ◆ Overall % time <70 mg/dL Exploratory: • Times in ranges-overall (70-180 mg/dL, >180 mg/dL, >250 mg/dL, 70-140 mg/dL) • Mean glucose

	• Overall variability (coefficient of variation (CV) and standard deviation (SD)) • Hemoglobin A1C (HbA1c) change from baseline • CGM metrics for hypoglycemia, hyperglycemia, and variability during daytime and nighttime
Inclusion Criteria	Key inclusion criteria were as follows: (1) age ≥18 years old and diagnosed with T1D for at least one year, (2) currently using CSII with any brand of insulin pump for at least three months, and planned to use at least one basal rate above 3 units/h with the study pump, and (3) hemoglobin A1c (HbA1c) <10.5%.
Exclusion Criteria	Key exclusion criteria were as follows: (1) more than one episode of severe hypoglycemia (needing assistance) or diabetic ketoacidosis (DKA) in the past six months, (2) pregnancy, (3) unstable dose of glucagon-like peptide-1 (GLP-1) receptor agonist, sodium-glucose transport protein 2 (SGLT-2) inhibitor, or other medication for glycemic con- trol/weight loss in the last three months, (4) starting a new non-insulin glucose lowering or weight loss agent during the trial, (5) adrenal insufficiency, and (6) other chronic condition determined by investigator to interfere with participation in the study. The use of any insulin other than U-100 Lispro or Aspart was not allowed with the pump. Prior con- tinuous glucose monitoring (CGM) experience was not required.
Number of Enrolled Subjects	34 subjects
Study Population	Mean age was 39.9 ± 11.9 years, 41.2% were female, and diabetes duration was 21.8 ± 11.2 years. Mean TDI at enrollment was 1.2 units/kg per day with a range of 0.5 to 2.0 units/kg per day.
Study Methods	The study was a prospective, single-arm study of 13 weeks of home use of the the t:slim X2 insulin pump with Control-IQ+ technology in individuals with type 1 diabetes who planned to use at least one basal rate >3 units/hour, age 18 and older. Control-IQ+ technology removes the 3 unit/hour basal rate clipping that was present in earlier versions of Control-IQ technology, and allows for a wider range of weight and total daily insulin (TDI) input to the system. This study was designed to show the system functioned safely when used with user profile basal rates above 3 units/hr. Study participants were enrolled across 4 clinical study sites. After device training, participants used the system for 13 weeks. Exercise and meal challenges were performed during the study. Central laboratory HbA1c levels were collected at the start and end of the treatment period (study device use). Participants were also able to continue use of additional medications for glucose control and/or weight loss, such as SGLT-2 inhibitors, GLP-1 receptor agonists, or DPP-IV inhibitors, as long as on a stable dose.
Clinical Benefits	Use of the t:slim X2 insulin pump with Control-IQ+ technology, with removal of the 3 unit/hour basal rate clipping, was safe and effective in individuals with

	type 1 diabetes using basal rates >3 units/hour and high total daily insulin doses. HbA1c levels showed significant improvement from start to end of the 13-week treatment period, with a mean change of -0.82% and P-value <0.0001.
Undesirable Side-Effects or Adverse Events	There were no severe hypoglycemia or DKA events in the study. There were no adverse events during the study challenges. All challenges were completed safely.
Long-term Benefits and Risk	Long-term benefits and risk were not assessed as part of this study.
Limitations of Study	Limitations of the study include lack of a control arm, and as a safety study, the sample size was relatively small, making it difficult to examine any sub-groups.
Device Deficiency or Device Replacements due to Safety and/or Performance	There was only one instance of ketones due to infusion set failure that resolved with a backup injection per the study safety plan.

Table 8. Summary of Safety Evaluation of an Advanced Hybrid Closed Loop System Using Lyumjev with the Tandem t:slim X2 with Control-IQ in Adults, Adolescents and Children with Type 1 Diabetes

Study	Safety Evaluation of an Advanced Hybrid Closed Loop System Using Lyumjev with the Tandem t:slim X2 with Control-IQ in Adults, Adolescents and Children with Type 1 Diabetes (clinicaltrials.gov identifier: NCT05403502)
Subject Device	t:slim X2 insulin pump with Control-IQ+ technology, t:slim X2 3mL cartridge
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ+ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII).
Objective of Study	To evaluate the safety of Lyumjev (insulin lispro-aabc) use in the Tandem t:slim X2 insulin pump with Control-IQ+ technology in adult and pediatric participants with type 1 diabetes in an outpatient setting to support system labeling.
Study Design	Single-arm, multi-center, prospective clinical study for 13 weeks
Primary/Secondary Endpoints	Primary Safety Endpoints: • Severe hypoglycemia (Severe hypoglycemia is defined as having cognitive impairment such that assistance of another individual is needed for treatment)

	• Diabetic ketoacidosis (DKA) • Unanticipated adverse device effects • Other serious adverse events • Adverse drug reactions Secondary Safety Endpoints • All adverse events • CGM hypoglycemia outcomes: 24 hour and during postprandial periods for announced meals, excluding meal challenges described separately below • % time <54 mg/dL • % time <70 mg/dL • Rate of hypoglycemia events, defined as 15 or more consecutive minutes <54 mg/dL Other exploratory outcomes included CGM-measured postprandial glycemic peak, various other CGM-based measures of glycemic control, HbA1c, insulin delivery metrics, and patient-reported outcome questionnaires.
Inclusion Criteria	1. Age 6 to <81 years 2. Diagnosis of type 1 diabetes for at least 1 year 3. Currently using Control-IQ technology for at least 3 months, with CGM data recorded indicative of system use (active closed loop) for ≥85% of the possible time in 14 days prior to enrollment 4. Total daily insulin dose (TDD) at least 2 U/day 5. HbA1c < 10.5% 6. Residing full-time in the United States, with no anticipated travel outside the United States during the period of study participation. 7. For participants <18 years old, living with one or more parent/legal guardian knowledgeable about emergency procedures for severe hypoglycemia and able to contact the participant in case of an emergency, and willing to use the Dexcom Follow app (with push notifications turned on) for the duration of the study. 8. If >18 years old, participant has someone who lives within 30 minutes of them who is willing to be contacted if the study team can't reach the participant in case of a suspected medical emergency. 9. Participant has agreed to participate in the study; and has read, understood and signed the informed consent form (ICF) and assent, if applicable; and has agreed to follow all study procedures, including: • suspending use of any personal CGM for the duration of the clinical trial once the study CGM is in use • switching to or continuing to use Humalog during the lead-in period • switching to Lyumjev for the main study period. • willing and able to perform the study exercise and meal challenges. 10. Investigator has confidence that the participant can successfully operate all study devices and is capable of adhering to the protocol, including ability to respond to alerts and alarms, and to provide basic diabetes self-management. 11. Participant and/or parent/legal guardian have the ability to read and understand English

Exclusion Criteria	Key exclusion criteria were a severe hypoglycemia (SH) event or diabetic ketoacidosis (DKA) in the prior 6 months, or a medical or other condition considered to be a safety concern by the site investigator.
Number of Enrolled Subjects	179 completed the Humalog run-in and initiated Lyumjev insulin, and 173 completed the 13 week visit post-Lyumjev initiation.
Study Population	Participants initiating Lyumjev use ranged in age from 6 to 75 years (109 were <18 years old and 70 were ≥18 years old); 166 (95%) were White and 12 (7%) were of Hispanic ethnicity. Mean HbA1c was 7.2% +/-0.9.
Study Methods	The study had 2 periods: Humalog Lead-In Period (~16 days) and Lyumjev Treatment Period (13 weeks). Participants initiated a Humalog Lead-In Period of ~16 days. Participants who successfully completed the Humalog Lead-In Period, indicated by 85% of active closed-loop use during this period, were trained on the use of the study pump with Lyumjev and initiated the Lyumjev Treatment Period for 13 weeks. Participants were asked to perform 1 missed meal bolus and 1 exercise challenge at home during the Humalog Lead-in Period, then 3 meal and 3 exercise at-home challenges during the Lyumjev Treatment Period. A phone or videoconference contact occurred at 3 days (±1 day) after initiation of closed-loop system use with Lyumjev. Additional phone/videoconference contacts occurred at 1 week (±2 days), 2 weeks (±2 days), 3 weeks (±7 days), and 9 weeks (±7 days). A clinic visit occurred at 6 weeks (±7 days) and the final clinic visit at 13 weeks (91-98 days). HbA1c was measured at a central lab at the end of the Humalog Lead-in Period and at the end of the Lyumjev Treatment Period (13-week visit). Questionnaires were completed at screening and the 13-week visit.
Clinical Benefits	Use of Lyumjev in the Tandem t:slim X2 insulin pump with Control-IQ+ technology was well tolerated with few adverse effects and no increase in hypoglycemia. Rates of severe hypoglycemia and DKA were lower than in the T1D Exchange clinic registry data, with the statistical comparison meeting the prespecified success criteria. The safety of the Lyumjev insulin was maintained while achieving high time in range and a slight reduction in hyperglycemia compared with Humalog insulin and improved quality of life measures compared with study entry. Therefore, this trial demonstrated that Lyumjev use in the Tandem t:slim X2 insulin pump with Control-IQ+ technology was safe for adult and pediatric participants with type 1 diabetes.
Undesirable Side-Effects or Adverse Events	No SH events occurred during the 16-day lispro period. During the 13-week Lyumjev period, three SH events occurred in three participants (one in the adult cohort and two in the pediatric cohort), one of which was associated with seizure or loss of consciousness. None of the events was judged device-related. One event occurred because of manually bolusing and not eating,

	one after exercise and overriding the bolus calculator from a recommendation of zero units to instead a manual bolus of 1.5 units, and the third after manually bolusing before exercising when the blood glucose (BG) was still 60 mg/dL. The overall rate of SH events was 6.6 per 100 person-years, and the rate of SH associated with seizure or loss of consciousness was 2.2 per 100 person-years. The percentage of participants with at least one SH event requiring third-party assistance was 1.7% and the percentage of participants with SH associated with seizure or loss of consciousness was 0.6% compared with the age-matched frequency of 6.1% with at least one SH event associated with seizure or loss of consciousness during a 3-month period in the T1D Exchange registry (P = 0.07 comparing 1.7% vs. 6.1% and P = 0.02 comparing 0.6% vs. 6.1%). No cases of DKA occurred during the lispro period or the Lyumjev period. In the T1D Exchange clinic registry, 2.8% of age-matched participants reported a DKA event during a 3-month period (P = 0.04 comparing 0% vs. 2.8%).
Long-term Benefits and Risk	Long-term benefits and risk were not assessed as part of this study.
Limitations of Study	The trial did not have a concurrent, randomized control group and the comparison of glycemic endpoints using Lyumjev was made with a short period of lispro use preceding Lyumjev use. The study cohort consisted of existing Control-IQ users and had too few minoritized participants and participants with lower socioeconomic status (SES) to evaluate whether infusion-site reactions and other safety endpoints might differ by race, ethnicity, or SES. For an evaluation of the key safety metrics (SH and DKA), comparisons were made with retrospectively collected data from T1D Exchange clinic registry, a real-world cohort that likely differs from a clinical trial cohort, and for which data were collected at a time when the vast majority of persons with diabetes were not yet using HCL devices. As participants were not blinded to the insulin being used, it is possible that some of the effects seen with Lyumjev, including the benefits observed on the PRO surveys, might be attributable to a study effect in conjunction with the use of the t:slim X2 insulin pump with Control-IQ+ technology
Device Deficiency or Device Replacements due to Safety and/or Performance	No severe adverse events were related to the device.

Table 9. Summary of Safety and Efficacy of Sustained Automated Insulin Delivery Compared With Sensor and Pump Therapy in Adults With Type 1 Diabetes at High Risk for Hypoglycemia: A Randomized Controlled Trial

Study	Safety and Efficacy of Sustained Automated Insulin Delivery Compared With Sensor and Pump Therapy in Adults With Type 1 Diabetes at High Risk for Hypoglycemia: A Randomized Controlled Trial (clinicaltrials.gov identifier: NCT04266379)
Subject Device	t:slim X2 insulin pump with Control-IQ technology, t:slim X2 3mL cartridge

Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII).
Objective of Study	To assess the safety and efficacy of the t:slim X2 insulin pump with Control-IQ technology in adults with type 1 diabetes (T1D) at high risk for hypoglycemia.
Study Design	Prospective, randomized, controlled, multicenter study
Primary/Secondary Endpoints	The primary outcome was change in CGM-measured TBR (CGM percent time [%time] <70 mg/dL) from baseline. The key secondary outcomes, tested in a hierarchical fashion to preserve statistical significance, included CGM-measured time in target range (TIR; 70–180 mg/dL), time above range (TAR), mean sensor glucose (SG) reading, and percentage of CGM time with glucose level <54 mg/dL. If a nonsignificant comparison was encountered, all subsequent comparisons in the hierarchical list were considered exploratory. Key safety outcomes included the frequency of severe hypoglycemia and diabetic ketoacidosis.
Inclusion Criteria	1. Age >18 years old 2. Clinical diagnosis of T1D >1 year. 3. HbA1c <10/5% 4. Insulin administered by insulin pump for >6 months 5. Trained in carbohydrate counting 6. Clarke score >3, and/or experience of severe hypoglycemia during the previous 6 months. 7. Confirmed time below range (TBR; defined as sensor glucose [SG] reading <70 mg/dL) of ≥5% during the 2 week run-in period with blinded CGM.
Exclusion Criteria	1. Positive pregnancy test in female participants of child-bearing potential 2. Any associated chronic disease of therapy (except insulin) affecting glucose metabolism 3. Use of sodium-glucose cotransporter 2 inhibitors in the previous 3 months 4. Lack of any social or familial support able to intervene in case of severe hypoglycemic episode
Number of Enrolled Subjects	72
Study Population	Adults with T1D at high risk for hypoglycemia (defined as a Clarke score >3 and TBR of ≥5%) and/or a history of severe hypoglycemia.

Study Methods	Parallel-arm, randomized trial (2:1) of AID (t:slim X2 insulin pump with Control-IQ technology) versus CGM and pump therapy for 12 weeks. An optional 12-week extension with AID was offered to all participants.
Clinical Benefits	This parallel RCT exclusively focuses on adults with T1D at high risk for hypoglycemia, a poorly investigated population with AID systems, and successfully demonstrates that the t:slim X2 insulin pump with Control-IQ technology's superiority relative to sensor-augmented insulin pump therapy during the 12-week randomization phase and 12-week extension phase. The change in TBR (primary outcome) from baseline through the 12-week study intervention was significantly different between the study groups, with a decrease of −3.7 percentage points with AID (n=49) vs S&P (n=22). Changes in TIR and TAR (secondary outcomes) were also significantly different between the two study groups, with an increase in TIR of +8.6% and a decrease in TAR of −5.3% related to AID effect. During the 12-week extension, the effects of AID were sustained in the AID group and reproduced in the sensor augmented pump group. These data show the sustainability of the effects of AID use for 24 weeks and the reproducibility of these effects by those newly exposed to AID.
Undesirable Side-Effects or Adverse Events	Two severe hypoglycemic events occurred during the run-in period, including one leading to study withdrawal. One severe hypoglycemia event and two events of hyperglycemia with ketosis occurred in the AID group during the training phase while AID was still not activated. Two severe hypoglycemia events, two ketoacidosis events (including one in the extension phase, which led to the patient leaving the study), and one episode of hyperglycemia >300 mg/dL with no ketosis occurred while AID was in use. All hyperglycemic events, with or without ketosis or ketoacidosis, were related to infusion-catheter occlusions. Two severe adverse events occurred under AID but were not related to diabetes.
Long-term Benefits and Risk	Long-term benefits and risk were not assessed as part of this study.
Limitations of Study	Short study duration/exposure to AID therapy, trial was performed in university hospitals with dedicated and trained staff to support participants which may not reflect real life practice in typical outpatient settings. Only 6 participants had HbA1c ≥8% at baseline, indicating conclusions may not apply to people who experience both frequent/severe hypo and high HbA1c concurrently.

Table 10. Summary of Control-IQ Outcomes Comparing Dexcom G6 and G7 Sensors in Adults with Type 1 Diabetes

Study	Control-IQ Outcomes Comparing Dexcom G6 and G7 Sensors in Adults with Type 1 Diabetes
Subject Device	t:slim X2 insulin pump with Control-IQ technology, t:slim X2 3mL cartridge, Tandem t:slim mobile application
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices.

	Control-IQ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII). The Tandem t:slim mobile application is an accessory intended for use as a connected software device that is able to reliably and securely communicate with compatible insulin pumps, including receiving and displaying pump information and sending insulin delivery commands to a user's connected and compatible t:slim X2 insulin pump.
Objective of Study	To analyze real-world results from Dexcom G7 users who paired their sensor to the t:slim X2 insulin pump with Control-IQ technology.
Study Design	Retrospective Analysis, Single Center
Primary/Secondary Endpoints	The analysis included percent time CGM was active, percent time in closed loop, and standard CGM metrics (percent time 70-180 mg/dL, 70-140 mg/dL, <70 mg/dL, <54 mg/dL, >180 mg/dL, >250 mg/dL, mean glucose, glucose standard deviation, glucose coefficient of variation, and Glycemia Risk Index) between Dexcom G6 and Dexcom G7 use when used with the t:slim X2 insulin pump with Control-IQ technology.
Inclusion Criteria	Participants had to be adults (age ≥ 18 years of age) and prior t:slim X2 insulin pump with Control-IQ technology users. Participants had to be prior Dexcom G6 users with at least 30 days of G6 data with active Control-IQ technology use available directly before starting Dexcom G7 with the t:slim X2 insulin pump with Control-IQ technology, as well as 30 days of G7 data with active Control-IQ technology use directly after starting G7 with the t:slim X2 insulin pump with Control-IQ technology, to be defined as an active Control-IQ technology user.
Exclusion Criteria	Users of other supported CGM sensors were not included.
Number of Enrolled Subjects	463
Study Population	463 adults (mean age 36±15 years, 59% female, prior duration of Control-IQ use 4±2 years) started using Dexcom G7 paired with the t:slim X2 insulin pump with Control-IQ technology between November 2023 through June 2024 after previously using Dexcom G6 with their Tandem pump, and had at least 30 days of Control-IQ data available before and after starting G7 use.
Study Methods	Data analysis was performed based on data from insulin pumps downloaded to the Tandem t:connect and Tandem Source data management system from patients identified at the Barbara Davis Center Adult Endocrinology Clinic. Results were listed for the 30 days of Dexcom G7 use with Control-IQ technology after starting G7.
Clinical Benefits	Median time of sensor use and median time in closed loop were very high with use of each sensor. Median time in range 70-180 mg/dL was 70.7%

	during G6 use and 71.1% during G7 use with the t:slim X2 insulin pump with t:slim X2 insulin pump with Control-IQ technology, showing that most of the individuals met the consensus goal of >70% time in range. Most individuals also met consensus goals for time <70 mg/dL and time <54 mg/dL.
Undesirable Side-Effects or Adverse Events	None reported.
Long-term Benefits and Risk	Long-term benefits and risk were not assessed as part of this study.

5.2. Summary of Clinical Data from Other Sources

An overview of the systematic literature review carried out by Tandem is included in the clinical evaluation report. The review yielded several articles in which the Tandem Mobi Insulin Pump with Control-IQ+ technology, or the equivalent device, with associated accessories, was used. These articles reported Control-IQ technology met the expectations for performance and safety. The studies did not report additional adverse events or undesirable side-effects outside of the residual risks outlined above and in the Instructions for Use.

There has been no additional clinically relevant information obtained from the implementation of the Post Market Clinical Follow-up (PMCF) and Post Market Surveillance (PMS) plans. There have been no new or changed likelihood of an undesirable side-effect(s), or significant increase in the frequency or severity of incidents, or any identified trends, or any other main findings from the PMCF evaluation report or Periodic Safety Update Report.

Analysis of clinical data from the MAUDE database has been collected as part of the clinical evaluation process. The MAUDE database houses reports of adverse medical device events that are reported to the United States FDA by mandatory reporters such as manufacturers. The majority of the reports are for the resolution of alarm conditions. Analysis of clinical data from the MAUDE database did not report additional adverse events or undesirable side-effects outside of the residual risks outlined above and in the Instructions for Use.

5.3. Overall Summary of Clinical Performance and Safety

The probable benefits of the Tandem Mobi Insulin Pump with Control-IQ+ technology is based on data collected in prospective randomized clinical trials, literature and nonclinical studies of the equivalent device conducted to support regulatory clearance for the equivalent device.

The Tandem Mobi insulin pump with Control-IQ+ technology, as well as the Tandem Mobi 2 mL cartridge, and Tandem Mobi Mobile App, are beneficial to patients since use of the devices allows users to improve time in target glucose range 70–180 mg/dL by at least 5% from prior therapy, achieve glucose time in target range 3.9-10 mmol/L (70-180 mg/dL) ≥70% and improve quality of life (QoL scores improving ≥8% compared to prior therapy). Further, users of the devices are able to achieve time <3.9 mmol/L below 4%, as is now recommended by international consensus guidelines.

5.4. Ongoing or Planned Post-Market Clinical Follow-up

There is a completed post-market clinical follow-up ('PMCF') study for Control-IQ technology. A summary of this PMCF study, also known as the 'CLIO Study,' is provided below**.** This study assessed the real world safety and effectiveness of the t:slim X2 insulin pump with Control-IQ technology. There were no emerging risks, complications, or unexpected device failures.

With the addition of the age two years and older age indication, an additional post-market clinical follow-up study is planned.

Table 11. Summary of the Control-IQ Observational (CLIO) Study

Study	Control-IQ Observational Post-Approval Study (CLIO) (clinicaltrials.gov identifier: NCT04503174)
Subject Device	t:slim X2 insulin pump with Control-IQ technology, t:slim X2 3mL cartridge, Tandem t:slim mobile application
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII). The Tandem t:slim mobile application is an accessory intended for use as a connected software device that is able to reliably and securely communicate with compatible insulin pumps, including receiving and displaying pump information and sending insulin delivery commands to a user's connected and compatible t:slim X2 insulin pump.
Objective of Study	<u>Primary Objective</u> Demonstrate, in a real-world setting, the safety of the t:slim X2 insulin pump with Control-IQ technology for the management of type 1 diabetes by assessing the rate of severe hypoglycemia (SH) and diabetic ketoacidosis (DKA) <u>Secondary Objective</u> Assess the impact on patients' glycemic outcomes and user experience in the real world, during the first 12 months of use.
Study Design	Observational Case-Control Study
Primary/Secondary Endpoints	<u>Primary Endpoints</u> • Incidence rates of severe hypoglycemia (SH) and diabetic ketoacidosis (DKA)

	• Safety of the automatic population of CGM readings into the bolus calculator of the Control-IQ system <u>Secondary Endpoints</u> • Glycemic Outcomes as a measure of efficacy of the Control-IQ system • Patient-reported satisfaction with and trust in the Control-IQ system, usability of the system, and sleep quality
Inclusion Criteria	• Patients with self-reported type 1 diabetes who have been prescribed the Control-IQ system. • At least 6 years of age • Using Humalog or Novolog insulin • For females, not pregnant or planning pregnancy in the next 12 months. • Agreement to use the t:slim X2 insulin pump with Control-IQ technology, and to continue use for at least 12 consecutive months after study enrollment. • Agree to provide HbA1c result, obtained within the 3-month period prior to enrollment. • Ability to respond to alerts and alarms, and to provide basic diabetes self-management. • Patients who reside full-time in the United States. • Willingness to download the t:connect Mobile application to their Smartphone and keep it active throughout the study. Patients unable to use t:connect Mobile application must be willing to manually upload their insulin pump data to t:connect every three months and at the completion of the study. • Subject has read, understood and agreed to participate in the study, and has electronically signed the Informed Consent Form (ICF).
Exclusion Criteria	• Self-reported type 2 diabetes • < 6 years of age • Use of any glucose-lowering therapy other than Humalog or Novolog insulin • Inability to respond to alerts and alarms, or to provide basic diabetes self-management. • Pregnancy • Subjects who have not signed the ICF.
Number of Enrolled Subjects	A total of 3,157 individuals met enrollment criteria and started the monthly surveys. 2,998 participants completed the study.
Study Population	Median participant age was 29.0 (16.0-45.0) years. 55.7% were female. Last reported A1c prior to enrollment was 7.7 (6.9-8.7) % [61 (52-72) mmol/mol]. 2,190 participants (69.4%) were adults. 38.4% were prior Tandem pump users, 31.5% prior pump users of a different brand, and 30.1% were prior MDI

	users. The vast majority (87.2%) reported at least some prior CGM experience.
Study Methods	Single Arm, Observational Cohort Study
Clinical Benefits	For the primary outcome, Adverse events rates for both severe hypoglycemia and DKA with use of Control-IQ technology over the 12 months period were significantly lower for both adults and children compared to historically reported data. For adults, the observed rate of severe hypoglycemia was 9.77 (36.97) for Control-IQ use versus 29.45 (104.54) for the historical data from the T1D Exchange (Effect Size d=0.53, p<0.01), while for children the observed rate of severe hypoglycemia was 9.31 (34.31) for Control-IQ use versus 19.31 (85.73) for the historical data (Effect Size d=0.29, p<0.01). For adults, the observed rate of DKA was 1.46 (13.10) for Control-IQ use versus 9.81 (61.87) for the historical data from the T1D Exchange (Effect Size d=0.64, p<0.01), while for children the observed rate of DKA was 1.93 (13.78) for Control-IQ use versus 12.81 (70.43) for the historical data (Effect Size d=0.79, p<0.01). The percentage of boluses using the auto-population feature resulted in fewer readings <54 mg/dL (<3.0 mmol/L) and <70 mg/dL (<3.9 mmol/L) than those not using the feature, in every pre-bolus glucose range examined. This was examined for glucose ranges prior to bolus of 70-180 mg/dL, 181-250 mg/dL, >250 mg/dL, and overall. There was no evidence of increased risk of hypoglycemia when auto-populated CGM results were used to calculate the subsequent bolus versus manual entry of glucose levels into the bolus calculator. For the secondary outcome, glycemic outcomes, users of the system achieved international consensus guideline goals for time in range. Time in range 70-180 mg/dL (3.9-10.0 mmol/L) was 70.1% (61.0-78.8) for adults, 61.2% (52.4-70.5) for age 6-13, 60.9% (50.1-71.8) for age 14-17, and 67.3% (57.4-76.9) overall. For the secondary outcomes, patient-reported satisfaction with and trust in the Control-IQ System, usability of the system, and sleep quality, a theme of reduction in diabetes burden and improved sleep, along with high satisfaction, was consistently reported. 72.1% of participants used the Tandem t:slim mobile application to upload data for analysis, showing high rates of mobile app use.
Undesirable Side-Effects or Adverse Events	Rates of severe hypoglycemia and DKA were lower than historical rates.
Long-term Benefits and Risk	Long-term benefits and risk were not assessed as part of this study.
Limitations of Study	This study had limitations. First, it used different methodology than prior studies to define SH and DKA, potentially increasing reported AE rates in the

	study. Rates for these AE's as determined by T1D exchange surveys required loss of consciousness or seizure for SH, or overnight hospitalization for DKA, more stringent than our requirements. AE's were also self-reported, which could lead to inaccuracies in the reported information. Baseline survey AE's were not verified, and thus could not be used for comparison by the same methodology. The study did not include a run-in period of blinded CGM before Control-IQ use, or a control group, that would have offered a better comparison for AE rates. Individuals today are able to choose a variety of automated insulin delivery systems and CGMs that were not available during the time period of the T1D Exchange historical cohort. As such, there is a limitation in directly comparing rates to a cohort with a differing set of baseline therapy choices. In addition, there was a wide range for the standard deviation of reported events in all categories for both the historical data and Control-IQ use. Finally, the question of a ''digital divide'' of who could participate and upload remotely, and whether this could exclude individuals, remains open.
Device Deficiency or Device Replacements due to Safety and/or Performance	No UADE's were reported.

There is an ongoing PMCF study for the t:slim X2 insulin pump with Control-IQ+ technology Tandem Mobi insulin pump with Control-IQ+ technology in children age 2 to <6 years old with type 1 diabetes. A summary of the plan for this study is provided below. The study began enrollment in 2025.

Table 12. Summary of PS230005 Post-Approval Study

Study	PS230005 Post-Approval Study (clinicaltrials.gov identifier: NCT06717451)
Subject Device	t:slim X2 insulin pump with Control-IQ+ technology, Tandem Mobi insulin pump with Control-IQ+ technology, t:slim X2 3mL cartridge, Tandem Diabetes Care 2mL cartridge, Tandem t:slim mobile application, Tandem Mobi mobile application
Intended Use of Device	The t:slim X2 insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. The Tandem Mobi insulin pump is intended for the subcutaneous delivery of insulin, at set and variable rates, for the management of diabetes mellitus in persons requiring insulin. The pump is able to reliably and securely communicate with compatible, digitally connected devices. Control-IQ+ technology is intended for use with a compatible continuous glucose monitor (CGM) and the t:slim X2 insulin pump to automatically increase, decrease, and suspend delivery of basal insulin based on CGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold.

	The t:slim X2 3mL cartridge is indicated for use with the t:slim X2 System for the Continuous Subcutaneous Delivery of Insulin (CSII). The Tandem Diabetes Care 2 mL cartridge is intended for use with the Tandem Mobi insulin pump for the Continuous Subcutaneous Delivery of Insulin (CSII). The Tandem t:slim mobile application is an accessory intended for use as a connected software device that is able to reliably and securely communicate with compatible insulin pumps, including receiving and displaying pump information and sending insulin delivery commands to a user's connected and compatible t:slim X2 insulin pump. The Tandem Mobi mobile application allows a user to connect a compatible smartphone to the pump, using Bluetooth® wireless technology, to view data from the Tandem Mobi pump and perform pump functions directly on the user's smartphone. The Tandem Mobi mobile app also provides messages and alerts from the Tandem Mobi pump as push notifications on the user's smartphone. The Tandem Mobi mobile app can transmit pump and therapy data from the pump to the cloud as long as the user's smartphone is connected to the Internet.
Objective of Study	<u>Primary Objective</u> Demonstrate, in a real-world setting, the safety of the t:slim X2 insulin pump with Control-IQ+ technology or the Tandem Mobi insulin pump with Control-IQ+ technology for the management of type 1 diabetes by assessing the rate of severe hypoglycemia (SH) and diabetic ketoacidosis (DKA). <u>Secondary Objective</u> Demonstrate, in a real-world setting, the effectiveness of the t:slim X2 insulin pump with Control-IQ+ technology for the management of type 1 diabetes by assessing the impact on patients' glycemic outcomes and user experience in the real world, during the first 12 months of use.
Study Design	Observational Case-Control Study
Primary/Secondary Endpoints	<u>Primary Endpoints</u> • Incidence rates of severe hypoglycemia (SH) and diabetic ketoacidosis (DKA) <u>Secondary Endpoints</u> • Glycemic Outcomes as a measure of efficacy of the Control-IQ+ system • Patient-reported satisfaction with and trust in Control-IQ+ technology, usability of the system, and improved quality of life.
Inclusion Criteria	• Self-reported type 1 diabetes who have been prescribed the t:slim X2 insulin pump with Control-IQ+ technology or Tandem Mobi insulin pump with Control-IQ+ technology • Age 2 to <6 years at time of screening

	• Using an insulin approved for use in the pump • Using an iCGM sensor approved for use with the pump • Agreement to use Control-IQ+ technology, and to continue use for at least 12 consecutive months after study enrollment. • Agree to provide HbA1c result, obtained within the 6-month period prior to enrollment. • Ability for parent/guardian to respond to alerts and alarms, and to provide basic diabetes self-management. • Reside full-time in the United States. • Willingness to download the Tandem t:slim mobile application to their smartphone and keep it active throughout the study if using a Tandem t:slim X2 pump. Participants who are unable to use the Tandem t:slim mobile application must be willing to manually upload their insulin pump data to Tandem Source every three months and at the completion of the study. • Participant's parent/guardian has read, understood and agreed to participate in the study, and has electronically signed the Informed Consent Form (ICF).
Exclusion Criteria	• Use of any glucose-lowering therapy other than insulin. • A medical or other condition, or medications being taken that in the investigator's judgement would be a safety concern for participation in the study.
Number of Enrolled Subjects	Recruitment is ongoing.
Study Population	The study will recruit up to 180 participants, with a goal of a minimum of ~120 completers.
Study Methods	Single Arm, Observational Cohort Study

A summary of the safety and clinical performance of the device, intended for patients, is given below.

6. Overview for Patients

This section explains how the Tandem insulin pump has been determined to be safe and effective in patients taking insulin for diabetes treatment.

Please contact your doctor with any questions about the use of an insulin pump. Always follow the insulin pump User Guide instructions for safe use of the pump.

6.1. Clinical Background of the Device

The American Diabetes Association recommends treating diabetes with multiple daily injections or an insulin pump. Using an insulin pump with a continuous glucose monitoring device (CGM) is more advanced but also recommended (for example, a Dexcom CGM). When using a Tandem insulin pump with a CGM, other tools may be used to help decide when insulin should be delivered.

Control-IQ+ technology is a tool that a Tandem insulin pump can use to make decisions for you. A decision might be to increase, decrease or stop insulin delivery. Control-IQ+ uses information from the CGM to make these decisions for you on the pump.

The Tandem Mobi pump has a smartphone app that lets you see pump information and make insulin delivery decisions.

6.2. Safety

Risks of using an insulin pump

There are risks to taking insulin. There are some added risks from using an insulin pump. Following the instructions in the pump User Guide are important for safe use. Talk to your doctor about these risks.

Taking the wrong amount of insulin can raise or lower blood sugar to harmful levels. Possible added risks from using insulin pumps include:

- Infection at the site of the insulin infusion. Signs of infection are bleeding, pain, redness and skin discomfort at the site of the insulin infusion.
- Allergic reaction or skin discomfort from the sticky part of the infusion set used with the insulin pump.

How Tandem tests for safe pump use in patients

Tandem Diabetes Care Inc. puts all its devices through testing to make sure the devices are safe to use by a wide variety of people. Tandem also runs clinical studies on a regular basis to make sure the pump remains safe and effective. These studies look at the risks and benefits of using a Tandem insulin pump with a CGM and Control-IQ.

Contact your doctor if you don't like your experience using an insulin pump. Contact your doctor if you are concerned about using an insulin pump.

6.3. Suggested Profile and Training for Users

Tandem puts all its devices through a process called human factors testing. This process makes sure that a device is safe to use by a wide variety of people. Tandem's human factors process follows global standards for medical devices.

This testing showed that all Tandem insulin pump users need to do the following:

- Follow the instructions from your doctor. They will provide the right training for you.
- Follow the instructions from your Tandem pump Trainer.
- Follow the instructions in your insulin pump User Guide and your CGM User Guide.
- Monitor your glucose.
- Have good vision and/or hearing to recognize all functions of your Tandem pump and mobile app, including alerts, alarms, and reminders.

The table below provides a summary of eleven (11) completed clinical studies on people using the t:slim X2 Insulin Pump with Control-IQ (or Control-IQ+) technology. All eleven (11) studies found the insulin pump was a safe and effective way to deliver insulin. The Tandem Mobi pump is very similar to the Tandem t:slim X2 pump.

Table 13. Summary of Clinical Studies

Clinical Study	Summary
1. The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas, A Pivotal Study of t:slim X2 with Control-IQ Technology	This study looked at the safety and efficacy of the t:slim X2 insulin pump with Control-IQ technology in 168 people. The participants were 14 years of age or older and had type 1 diabetes. The participants either used a t:slim X2 insulin pump with Control-IQ technology or a Sensor Augmented pump for 6 months. The t:slim X2 insulin pump with Control-IQ technology was found to be safe and effective during 6 months of use. This study was completed in 2019.
2. The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas, Extension Phase, A Study of t:slim X2 with	This is an extension study to the trial mentioned above with 164 people from the original study. The participants continued using the t:slim X2 insulin pump with Control-IQ technology or switched to Basal-IQ technology for 3 more months. The participants who used Control-IQ had better time in target range and HbA1c compared to Basal-IQ. The t:slim X2

Control-IQ Technology	insulin pump with Control-IQ technology was found to be safe and effective during 9 months of total use. This study was completed in 2020.
3. The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas in Pediatrics, A Study of t:slim X2 with Control-IQ Technology	This study looked at the safety and efficacy of the t:slim X2 insulin pump with Control-IQ technology in 101 children with type 1 diabetes ages 6 to 13. The participants used t:slim X2 insulin pump with Control-IQ or a Sensor Augmented insulin pump for 16 weeks. The participants who used Control-IQ had more time in target range compared to Sensor-Augmented pump. The t:slim X2 insulin pump with Control-IQ technology was found to be safe and effective. This study was completed in 2020.
4. The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas in Pediatrics, Extension Phase, A Study of t:slim X2 with Control-IQ Technology	This is an extension study to the trial mentioned above. The participants who used the t:slim X2 insulin pump with Control-IQ technology in the original study continued using Control-IQ for 12 more weeks. Participants who used a Sensor-Augmented pump switched to Control-IQ. The participants who used Control-IQ had more time in target range and less time in hyperglycemia compared to Sensor-Augmented pump. The t:slim X2 insulin pump with Control-IQ technology was found to be safe and effective during 28 weeks of total use. This study was completed in 2020.
5. The Pediatric Artificial Pancreas (PEDAP) trial: A Randomized Controlled Comparison of the Control-IQ technology Versus Standard of Care in Young Children in Type 1 Diabetes	This study assessed the safety and efficacy of the t:slim X2 insulin pump with Control-IQ technology in children with type 1 diabetes ages 2 to 6 years old. The participants used the t:slim X2 insulin pump with Control-IQ technology or their usual insulin therapy with CGM for 3 months. Participants using Control-IQ had more time in target range compared to the group who used their usual insulin therapy with CGM. Results also showed Control-IQ was safe to use in this age group. This study was completed in 2022.
6. The Pediatric Artificial Pancreas (PEDAP) trial: A Randomized Controlled Comparison of the	This was a 13-week extension study of the trial above. Participants were interviewed on their experience using t:slim X2 insulin pump with Control-IQ+ technology. Results showed that use of the Control-IQ+ system in children led to improvements in mental health and less burden for families. The participants reported a more positive

Control-IQ technology Versus Standard of Care in Young Children in Type 1 Diabetes (Extension Phase)	user experience with Control-IQ+ compared to their usual insulin therapy. They also highlighted benefits of Control-IQ+ beyond glycemic outcomes. This study was completed in 2023.
7. Control-IQ Technology for High Insulin Users with Type 1 Diabetes (Higher-IQ)	This study assessed the safety and efficacy of the t:slim X2 insulin pump with Control-IQ+ technology in adults with type 1 diabetes. The participants had to use at least one basal rate over 3 units/hour. The t:slim X2 insulin pump with Control-IQ+ technology was found to be safe and effective during the 13-weeks of use. This study was completed in 2023.
8. Safety Evaluation of an Advanced Hybrid Closed Loop System Using Lyumjev with the Tandem t:slim X2 with Control-IQ in Adults, Adolescents and Children with Type 1 Diabetes	This study evaluated the safety of Lyumjev insulin in the t:slim X2 insulin pump with Control-IQ+ technology in adults and children with type 1 diabetes. Participants used their Control-IQ+ system with Humalog insulin for 2 weeks followed by 13 weeks of Control-IQ+ system use with Lyumjev insulin. The use of the Control-IQ+ system with Lyumjev insulin was found to be safe and effective. Quality of life measures also improved compared with study entry. This study was completed in 2023.
9. Safety and Efficacy of Sustained Automated Insulin Delivery Compared With Sensor and Pump Therapy in Adults With Type 1 Diabetes at High Risk for Hypoglycemia: A Randomized Controlled Trial	This study evaluated the safety and efficacy of the t:slim X2 insulin pump with Control-IQ technology in adults with high risk for hypoglycemia. The participants used t:slim X2 insulin pump with Control-IQ or a Sensor-Augmented insulin pump for 3 months. Participants who used the Control-IQ system had significantly better time in the target range and less time in hypoglycemia compared to Sensor-Augmented pump. In the 3-month extension phase, participants who switched from Sensor-Augmented pump to Control-IQ saw the same improvements. This study was completed in 2021.
10. Control-IQ Outcomes Comparing Dexcom G6 and G7 Sensors	This real-world study followed 463 Tandem pump users before and after changing their glucose sensor. Participants were using Control-IQ technology with a Dexcom G6 sensor and switched to a Dexcom G7 glucose sensor.

in Adults with Type 1 Diabetes	Clinical outcomes were the same before and after changing sensors. Results showed Tandem pumps work just as well with both sensors. This study was completed in 2024.
11. Control-IQ Observational Post-Approval Study (CLIO)	This was a large post-market study with nearly 3,000 people who used Control-IQ for 12 months. Results showed Control-IQ users had lower rates of diabetic ketoacidosis and severe hypoglycemia compared to historical data. This was true for both adults and children. The t:slim X2 insulin pump with Control-IQ+ technology was found to be safe and effective during 12 months of use in the real-world. This study was completed in 2023.

7. Reference to Harmonized Standards and Common Specifications Applied

The following standards have been applied to the t:slim X2 insulin pump with Control-IQ+ technology and Tandem t:slim Mobile App:

- EN ISO 14971:2019/A11:2021 - Medical devices. Application of risk management to medical devices
- EN ISO 13485:2016/A11:2021 - Medical devices. Quality management systems. Requirements for regulatory purposes
- AAMI ES60601-1: 2005 & A1:2012 & A2:2021 - Medical electrical equipment-Part 1: General requirements for basic safety and essential performance (IEC 60601-1:2005, MOD)
- AAMI/IEC 60601-1-2:2014- Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests
- IEC 60601-1-6:2010/A2:2021 - Medical electrical equipment - Part 1-6: General requirements for basic safety and essential performance - Collateral standard: Usability (including IEC 62366-1:2015/(R2021) +AMD1:2020 – Medical devices - Part 1: Application of usability engineering to medical devices, including amendment 1)
- IEC 60601-1-8:2020 - Medical electrical equipment — Part 1-8: General requirements for basic safety and essential performance — Collateral standard: General requirements, tests and guidance for alarm systems in medical electrical equipment and medical electrical systems
- IEC 60601-1-11:2020 - Medical electrical equipment - Part 1-11: General requirements for basic safety and essential performance - Collateral Standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment

- IEC 60601-2-24:2012 - Medical electrical equipment - Part 2-24: Particular requirements for the basic safety and essential performance of infusion pumps and controllers
- IEC 60601-1-10:2008+A2:2021 - Medical electrical equipment - Part 1-10: General requirements for basic safety and essential performance - Collateral Standard: Requirements for the development of physiologic closed-loop controllers
- AAMI/IEC 62304:2006+A1:2016 - Medical device software — Software life cycle processes
- CEI EN 62366-1/A1- Medical devices Part 1: Application of usability engineering to medical devices
- ISO 10993-1:2020 - Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process
- ISO 10993-3:2014 - Biological Evaluation of Medical Devices Part 3: Tests for Genotoxicity, Carcinogenicity, and Reproductive Toxicity
- ISO 10993-4/Amd.1:2006 - Biological Evaluation of Medical Devices Part 4: Selection of tests for interactions with blood
- ISO 10993-5:2009 - Biological Evaluation of Medical Devices Part 5: Tests for in-vitro cytotoxicity
- ETSI EN 300 328 V2.2.2 (2019-08) - Wideband transmission systems; Data transmission equipment operating in the 2,4 GHz band; Harmonised Standard for access to radio spectrum
- ISO 11137-1:2006/Amd2:2018 - Sterilization of health care products — Radiation — Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices
- ISO 11137-2:2013/Amd1:2022 - Sterilization of health care products — Radiation — Part 2: Establishing the sterilization dose
- ISO 11737-1:2018/Amd1:2021 - Sterilization of health care products — Microbiological methods — Part 1: Determination of a population of microorganisms on products
- ISO 11737-2:2019 - Sterilization of health care products - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process
- EN ISO 15223-1:2021 - Medical devices. Symbols to be used with information to be supplied by the manufacturer

8. Revision History

SSCP Revision Number	Date Issued	Change Description	Revision Validated by the Notified Body
A	Dec 16, 2024	Initial Release	☐ Yes Validation Language: ☒ No

B	Mar 5, 2025	Updated to reflect validation by notified body. Edited language under patient sections to suit lay audiences, per MDCG guidance.	☒ Yes Validation Language: English ☐ No
C	Oct 2, 2025	Updated Warnings per BSI White Paper, “Guidance on MDCG 2019-9: Summary of Safety and Clinical Performance” to list those most relevant to patients and clinicians based on the available evidence. Additional simplification of patient sections per MDCG guidance. Updated standards testing.	☐ Yes Validation Language: ☒ No