510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K250798

B Applicant

Tandem Diabetes Care, Inc.

C Proprietary and Established Names

Control-IQ+ technology

D Regulatory Information

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

E. Purpose for Submission:

The purpose of this submission is to add Lyumjev U-100 insulin as a compatible insulin to the labeling of the subject device.

II Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

Control-IQ+ technology is intended for use with compatible integrated continuous glucose monitors (iCGM) and alternate controller enabled (ACE) pumps to automatically increase, decrease, and suspend delivery of basal insulin based on iCGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold.

Control-IQ+ technology is intended for the management of Type 1 diabetes mellitus in persons 2 years of age and greater and of Type 2 diabetes mellitus in persons 18 years of age and greater.

Control-IQ+ technology is intended for single patient use and requires a prescription.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Only use U-100 insulin analogs that have been tested and found to be compatible for use in the pump. Use of insulin with lesser or greater concentration can result in under delivery or over delivery of insulin. This can cause hypoglycemia (low BG) or hyperglycemia (high BG) events.

When the CGM reading is automatically populated into the bolus calculator, only the current CGM reading is used to calculate the correction bolus. The trend arrow is not used in the dose calculation. Speak with your healthcare provider for recommendations on how best to utilize the arrows for your correction bolus dosing.

Control-IQ+ 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 or who weigh less than 20 pounds, as those are the required minimum values needed in order for Control-IQ technology to operate safely.

The pump is magnetic resonance (MR) unsafe. You must take off your pump and leave it outside the procedure room.

DO NOT use Dexcom CGM readings to make diabetes treatment decisions or assess glucose control when taking hydroxyurea, a medication used in the treatment of diseases including cancer and sickle cell anemia. Hydroxyurea is known to interfere with glucose readings from the Dexcom sensor. Relying on sensor glucose values while taking hydroxyurea could result in missed hypoglycemia alerts or errors in diabetes management, such as giving a higher dose of insulin than necessary to correct falsely high sensor glucose values.

III Device Description:

The Subject Device, Control-IQ+ technology ("Control-IQ+") is a software-only device intended for the management of type 1 and type 2 diabetes mellitus. The device controls insulin delivery from a compatible alternate controller enabled insulin pump (ACE pump) based on inputs provided by a compatible integrated continuous glucose monitor (iCGM) and inputs provided by the user (e.g., carbohydrate intake, exercise, and sleep schedule). Control-IQ+ technology is meant to be installed on a compatible ACE pump.

Control-IQ+ technology has three different modes: Normal, Sleep, and Exercise. The glucose targets are not individually customizable in these modes but can change based on the mode selected. During Normal mode, Control-IQ+ technology aims to control glucose within a target range of 112.5 – 160 mg/dL, during Sleep mode the target range is 112.5 – 120 mg/dL, and during Exercise mode the target range is 140 – 160 mg/dL.

Control-IQ+ technology includes an integrated feature whereby iCGM values are automatically populated into the glucose field of the integrated bolus calculator when Control-IQ+ technology is active (i.e., the device is operating in closed-loop mode). This feature is disabled when Control-IQ is turned off.

Control-IQ+ technology requires users to input their weight and their total daily insulin requirement, which should be established with the help of a health care provider before using the device.

IV Substantial Equivalence Information:

A Predicate Device Name(s):
Control-IQ+ technology

B Predicate 510(k) Number(s):
K243823

C Comparison with Predicate(s):

Device & Predicate Device(s):	K250798	K243823
Device Trade Name	Control-IQ+ technology	Same
General Device Characteristic Similarities		
Intended Use/Indications For Use	Control-IQ+ technology is intended for use with compatible integrated continuous glucose monitors (iCGM) and alternate controller enabled (ACE) pumps to automatically increase, decrease, and suspend delivery of basal insulin based on iCGM readings and predicted glucose values. It can also deliver correction boluses when the glucose value is predicted to exceed a predefined threshold. Control-IQ+ technology is intended for the management of Type 1 diabetes mellitus in persons 2 years of age and greater and of Type 2 diabetes mellitus in persons 18 years of age and greater.	Same

	Control-IQ+ technology is intended for single patient use and requires a prescription.	
General Device Characteristic Differences		
Compatible Insulins	For Type 1 diabetes mellitus in persons 2 years of age and greater and Type 2 diabetes mellitus in persons 18 years of age and greater: NovoLog U-100 Insulin Humalog U-100 Insulin Lyumjev U-100 Insulin	For Type 1 diabetes mellitus in persons 2 years of age and greater and Type 2 diabetes mellitus in persons 18 years of age and greater: NovoLog U-100 Insulin Humalog U-100 Insulin

V Standards/Guidance Documents Referenced:

- Special controls established under 21 CFR 862.1356
- ANSI AAMI ISO 14971:2019 - "Medical devices - Applications of risk management to medical devices"

VI Performance Characteristics:

A Analytical Performance:

For the purposes of analytical and clinical validation testing, the Control-IQ algorithm was installed on the t:slim X2 Insulin Pump with Interoperable Technology ACE pump, which was paired with the Dexcom G6 Continuous Glucose Monitoring (CGM) system.

B Other Supportive Instrument Performance Characteristics Data:

Summary of Clinical Testing:
The sponsor conducted a prospective, multi-center, single-arm study to evaluate the safety of Lyumjev (insulin lispro-aabc) U-100 insulin 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. The Lyumjev Treatment Period was 13 weeks in duration.

A summary of the pivotal clinical study is provided in the following table:

Study Feature	Description
Title	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 (TL1)
Summary	The study design was a single-arm trial of existing pediatric and adult users of the Tandem t:slim X2 insulin pump with Control-IQ+ technology. Participants completed a ~16 day Humalog Lead-In

	Period using Humalog in the pump followed by a 13-week period using Lyumjev in the pump. At-home exercise and meal challenges were performed in both periods.
Investigational Device	t:slim X2 insulin pump with Control-IQ+ technology
Objectives	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 prospective safety trial
Number of Sites	14 clinical sites
Population	173 participants completed the study. The mean ± SD age at enrollment was 24 ± 17 years, mean HbA1c at the start of Lyumjev was 7.1% ± 0.9%, 50% of participants were female, and 95% were White. Key Inclusion Criteria: • Age 6 to <81 years • Diagnosis of Type 1 Diabetes for at least 1 year • Currently using Control-IQ technology for at least 3 months • Total daily insulin dose at least 2 U/day • HbA1c <10.5% Key Exclusion Criteria: • More than 1 episode of diabetic ketoacidosis or severe hypoglycemia (needing assistance) in the past 6 months • Concurrent use of any non-insulin glucose-lowering agent other than metformin
Sample Size	193 participants were enrolled in the study, 179 completed the Humalog run-in and initiated Lyumjev insulin, and 173 completed the 13 week visit post-Lyumjev initiation.
Treatment Groups	The study had 2 periods: Humalog Lead-In Period (~16 days) and Lyumjev Treatment Period (13 weeks).
Study Duration	Duration of treatment was about 15 weeks (~16 days of Humalog lead-in, and 13 weeks of Lyumjev treatment)
Protocol Overview/Synopsis	Informed consent was signed, and eligibility was assessed. Eligible participants who were using Control-IQ for at least 3 months 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.
Safety Results	During the Lyumjev Treatment Period there were 3 severe hypoglycemic events, 0 DKA events, 3 infusion site reactions reported as adverse events, 2 other adverse drug reactions reported as adverse events, and 2 serious adverse events other than severe hypoglycemia and DKA. The overall percentage of participants with at least 1 severe hypoglycemia event requiring third party assistance was 1.7% and the percentage of participants with severe hypoglycemia associated with seizure or loss of consciousness was 0.6%. For DKA, the overall percentage of participants with at least 1 DKA event was 0% in the Lyumjev treatment period.

Participant Demographics

	Overall N=179	**Pediatrics** N=109	**Adults** N=70
Age at Enrollment (years)			
mean ± standard deviation (SD)	24 ± 17	12 ± 3	43 ± 14
Range	6 to 75	6 to 17	18 to 75
Sex – Female (n (%))	90 (50%)	57 (52%)	33 (47%)
Weight (kg)			
mean ± SD	65 ± 26	51 ± 18	87 ± 21
Range	21 to 138	21 to 102	56 to 138
Body Mass Index at Enrollment (kg/m^2)			
mean ± SD	NA	NA	28.9 ± 5.9
Range			19.1 to 47.8
Race (n (%))[a]			
White	166 (95%)	97 (92%)	69 (99%)
Black/African American	1 (<1%)	1 (<1%)	0 (0%)
Asian	2 (1%)	2 (2%)	0 (0%)
Native Hawaiian/Pacific Islander	1 (<1%)	0 (0%)	1 (1%)

	Overall N=179	Pediatrics N=109	Adults N=70
American Indian/Alaskan Native	1 (<1%)	1 (<1%)	0 (0%)
More than One Race	4 (2%)	4 (4%)	0 (0%)
Ethnicity – (n (%))[a]			
Hispanic	12 (7%)	10 (9%)	2 (3%)
Non-Hispanic	165 (93%)	97 (91%)	68 (97%)
Highest Level of Education (n (%))[a,b]			
<Bachelor's Degree	49 (28%)	29 (27%)	20 (29%)
Bachelor's Degree	74 (42%)	43 (40%)	31 (44%)
Advanced Degree	55 (31%)	36 (33%)	19 (27%)
Annual Household Income (n (%))[a]			
<50K	14 (9%)	7 (7%)	7 (11%)
50K to <100K	43 (27%)	22 (23%)	21 (32%)
≥100K	105 (65%)	68 (70%)	37 (57%)
Health Insurance (n (%))[a]			
Private	143 (81%)	84 (78%)	59 (86%)
Medicare	8 (5%)	2 (2%)	6 (9%)
Medicaid	18 (10%)	17 (16%)	1 (1%)
Other Government	8 (5%)	5 (5%)	3 (4%)
None	0 (0%)	0 (0%)	0 (0%)

[a] 2 pediatric participants were missing ethnicity, 4 pediatric participants were missing race, 1 pediatric participant was missing education, 12 pediatric and 5 adult participants were missing income, and 1 pediatric and 1 adult participant were missing insurance.
[b] For pediatric participants, highest education of parent/guardian reported.

Participant Diabetes History

	Overall N=179	Pediatrics N=109	Adults N=70
Diabetes Duration at Enrollment (years)			
mean ± SD	14 ± 13	6 ± 3	27 ± 12
Range	1 to 57	1 to 15	3 to 57
Baseline HbA1c at End of Humalog Lead-In (%)			
mean ± SD	7.2 ± 0.9	7.2 ± 0.9	7.1 ± 0.9
Range	5.5 to 10.3	5.5 to 10.3	5.5 to 8.9
Humalog Period Total Daily Insulin (U)			

	Overall N=179	Pediatrics N=109	Adults N=70
mean ± SD	56 ± 32	52 ± 29	61 ± 36
Range	14 to 222	14 to 167	22 to 222
Humalog Period Total Daily Insulin (U/kg)			
mean ± SD	0.86 ± 0.32	0.99 ± 0.30	0.67 ± 0.26
Range	0.32 to 2.39	0.38 to 2.39	0.32 to 1.62

Safety Results

The primary endpoint evaluated the total number of safety events (severe hypoglycemia, diabetic ketoacidosis, unanticipated adverse device effects, adverse drug reactions, and other serious adverse events), number and proportion of participants who experienced at least one safety event, and the rate of events per 100 person years. The proportion of severe hypoglycemia (SH) and diabetic ketoacidosis (DKA) events were compared to proportions of events occurring in a similar time frame among participants enrolled in the T1D exchange. All participants who initiated the Lyumjev treatment and provided at least 24 hours of CGM data were included in the analyses.

During the Lyumjev Treatment Period there were 3 severe hypoglycemic events, 0 DKA events, 3 infusion site reactions reported as adverse events, 2 other adverse drug reactions reported as adverse events, and 2 serious adverse events other than severe hypoglycemia and DKA. In the Lyumjev Treatment Period, the overall percentage of participants with at least 1 severe hypoglycemia event requiring third party assistance was 1.7% and the percentage of participants with severe hypoglycemia associated with seizure or loss of consciousness was 0.6% compared with 6.1% with at least one severe hypoglycemia event associated with seizure or loss of consciousness during a 3-month period in the T1D Exchange registry when matched on age (P=0.07 and P=0.02, respectively, favoring Lyumjev). For DKA, the overall percentage of participants with at least 1 DKA event was 0% in the Lyumjev treatment period compared with 2.8% during a 3-month period in the T1D Exchange registry (P=0.04 favoring Lyumjev).

	Pediatrics (6-17 Years)		Adults (18+ Years)	
	Humalog Lead-In Period (N=109) # Events/# Participants with ≥1 Event	Lyumjev Treatment Period (N=109) # Events/# Participants with ≥1 Event	Humalog Lead-In Period (N=70) # Events/# Participants with ≥1 Event	Lyumjev Treatment Period (N=70) # Events/# Participants with ≥1 Event
All Adverse Events	25/19	124/64	8/7	61/37
Severe Hypoglycemia Events	0/0	2/2	0/0	1/1
Diabetic Ketoacidosis Events	0/0	0/0	0/0	0/0
Other Serious Adverse Events	0/0	1/1	0/0	1/1

	Pediatrics (6-17 Years)		Adults (18+ Years)	
	Humalog Lead-In Period (N=109) # Events/# Participants with ≥1 Event	Lyumjev Treatment Period (N=109) # Events/# Participants with ≥1 Event	Humalog Lead-In Period (N=70) # Events/# Participants with ≥1 Event	Lyumjev Treatment Period (N=70) # Events/# Participants with ≥1 Event
Other Adverse Events (Non-serious)	25/19	121/64	8/7	59/37
Hyperglycemia with or without ketosis related to study device	7/6	23/20	1/1	17/12
Hyperglycemia with or without ketosis not related to study device	2/2	4/4	2/2	2/1
Nonsevere hypoglycemia	0/0	0/0	0/0	0/0
Nonglycemic adverse events	16/15	94/52	5/4	40/29

	Overall N=179	Pediatrics (6-17 Years) N=109	Adults (18+ Years) N=70
Severe Hypoglycemic (SH) Events			
Number of SH Events per Participant			
0	176	107	69
1	3	2	1
2	0	0	0
Incidence Rate per 100 Person-Years	6.6	7.1	5.8
% of Participants with ≥1 SH event in Lyumjev Treatment Period	1.7%	1.8%	1.4%
% of Participants with ≥1 SH event in T1D Exchange [a]	6.1%	4.8%	7.4%
P-Value Comparing % of Participants with ≥1 SH event in Current Study vs. T1D Exchange	P = 0.07	P = 0.17	P = 0.11
Diabetic Ketoacidosis (DKA) Events			
Number of DKA Events per Participant			
0	179	109	70

1	0	0	0
2	0	0	0
Incidence Rate per 100 Person-Years	0.0	0.0	0.0
% of Participants with ≥1 DKA event: Control IQ+Lyumjev	0.0%	0.0%	0.0%
% of Participants with ≥1 DKA event: T1D Exchange [a]	2.8%	3.2%	2.5%
P-Value Comparing % of Participants with ≥1 DKA event in Control IQ+Lyumjev vs. T1D Exchange	P = 0.04	P = 0.09	P = 0.25
Lyumjev Adverse Drug Reactions (Not Including Infusion Site Reactions)			
Total Events	2	1	1
Incidence Rate per 100 Person-Years	4.4	3.6	5.8
% of Participants with ≥1 Event	1.1%	0.9%	1.4%
Infusion Site Reactions during Lyumjev Treatment Period			
Total Infusion Site Reactions *(# events/# participants with ≥1 event)*	445 / 101	153 / 55	292 / 46
Infusion Site Reactions Resulting in Adverse Event	3 (1%)	2 (1%)	1 (<1%)
Infusion Site Reactions Associated with Study Discontinuation	2 (<1%)	1 (1%)	1 (<1%)
Infusion Site Reactions per Participant			
0	78 (44%)	54 (50%)	24 (34%)
1	37 (21%)	24 (22%)	13 (19%)
≥2	64 (36%)	31 (28%)	33 (47%)

[a] T1D Exchange frequency reported from the following published article: *Foster et al. State of type 1 diabetes management and outcomes from the T1D Exchange in 2016-2018. Diabetes Technol Ther 2019; 21: 66-72*. In the T1D Exchange, an SH event required loss of consciousness or seizure and a DKA event required a diagnosis by a doctor and an overnight hospitalization. The overall percentage of participants with an event in the T1D Exchange was derived weighting by age group in the TL1 study.

Secondary safety endpoints included CGM hypoglycemia outcomes percentage of time <54 mg/dL, percentage of time <70 mg/dL, and rate of hypoglycemia events. Secondary safety CGM metrics comparing the Humalog lead-in period and Lyumjev treatment period by age group are shown below.

	Pediatrics (6-17 Years)		Adults (18+ Years)	
	Humalog Lead-In Period (N=109) Mean± SD	Lyumjev Treatment Period (N=109) Mean± SD	Humalog Lead-In Period (N=70) Mean± SD	Lyumjev Treatment Period (N=70) Mean± SD
24 Hours				
% Time < 54 mg/dL	0.28% ± 0.34%	0.31% ± 0.28%	0.26% ± 0.38%	0.19% ± 0.21%
% Time < 70 mg/dL	1.4% ± 1.3%	1.4% ± 1.0%	1.5% ± 1.3%	1.0% ± 1.0%
CGM Hypoglycemic Event Rate per Week[a]	0.46 ± 0.78	0.56 ± 0.59	0.46 ± 0.72	0.37 ± 0.45
Daytime (6:00 AM – 11:59 PM)				
% Time < 54 mg/dL	0.27% ± 0.35%	0.32% ± 0.30%	0.24% ± 0.40%	0.18% ± 0.23%
% Time < 70 mg/dL	1.6% ± 1.5%	1.5% ± 1.1%	1.3% ± 1.2%	1.1% ± 1.0%
CGM Hypoglycemic Event Rate per Week [a]	0.30 ± 0.58	0.44 ± 0.49	0.34 ± 0.61	0.28 ± 0.36
Nighttime (12:00 AM – 5:59 AM)				
% Time < 54 mg/dL	0.21% ± 0.46%	0.26% ± 0.31%	0.28% ± 0.51%	0.17% ± 0.21%
% Time < 70 mg/dL	1.0% ± 1.3%	0.9% ± 0.9%	1.6% ± 1.8%	0.8% ± 0.8%
CGM Hypoglycemic Event Rate per Week [a]	0.10 ± 0.26	0.10 ± 0.15	0.09 ± 0.23	0.08 ± 0.12
Postprandial % Time < 54 mg/dL[b]	**N=108**	**N=108**	**N=66**	**N=66**
≤1 Hour	0.16% ± 0.37%	0.42% ± 0.52%	0.14% ± 0.47%	0.16% ± 0.27%
≤2 Hours	0.31% ± 0.55%	0.48% ± 0.52%	0.15% ± 0.38%	0.22% ± 0.33%
>1-≤2 Hour	0.39% ± 0.71%	0.50% ± 0.57%	0.12% ± 0.34%	0.26% ± 0.45%
>2-≤4 Hour	0.18% ± 0.40%	0.22% ± 0.29%	0.28% ± 0.66%	0.19% ± 0.30%
≤4 Hours	0.27% ± 0.42%	0.36% ± 0.37%	0.23% ± 0.48%	0.21% ± 0.33%
Postprandial % Time < 70 mg/dL[b]	**N=108**	**N=108**	**N=66**	**N=66**
≤1 Hour	1.2% ± 1.6%	1.9% ± 1.8%	0.7% ± 1.6%	1.0% ± 1.3%
≤2 Hours	1.7% ± 1.9%	2.4% ± 1.9%	1.0% ± 1.5%	1.3% ± 1.5%
>1-≤2 Hour	2.1% ± 2.5%	2.8% ± 2.3%	1.3% ± 1.9%	1.7% ± 1.8%
>2-≤4 Hour	1.5% ± 1.7%	1.3% ± 1.3%	1.3% ± 1.7%	1.1% ± 1.2%
≤4 Hours	1.6% ± 1.6%	1.9% ± 1.4%	1.2% ± 1.5%	1.3% ± 1.3%

[a] Analytic Definition of a CGM-Measured Hypoglycemic Event: A hypoglycemic event was defined as 15 consecutive minutes with a sensor glucose value <54 mg/dL. The end of the

hypoglycemic event was defined as a minimum of 15 consecutive minutes with a sensor glucose concentration ≥70 mg/dL. When a hypoglycemic event ended, the study participant became eligible for a new event.
[b] Postprandial periods denote the time from a non-zero carb entry. 1 pediatric and 4 adult participants did not have sufficient postprandial CGM data to be analyzed.

Exploratory analyses included various CGM-based measures of glycemic control, HbA1c, and insulin delivery metrics, and patient-reported outcome questionnaires. Exploratory CGM metrics calculated during the daytime (06:00 AM to 11:59 PM), nighttime (12:00 AM to 5:59 AM), and overall, are summarized by age group below.

	Pediatrics (6-17 Years)		**Adults (18+ Years)**	
	Humalog Lead-In Period (N=109) Mean± SD	**Lyumjev Treatment Period (N=109) Mean± SD**	**Humalog Lead-In Period (N=70) Mean± SD**	**Lyumjev Treatment Period (N=70) Mean± SD**
24 Hours				
Time in Range 70-180 mg/dL (%)	62% ± 15%	64% ± 12%	69% ± 13%	70% ± 13%
Time in Range 70-140 mg/dL (%)	39% ± 15%	40% ± 13%	43% ± 12%	45% ± 13%
Time >180 mg/dL (%)	36% ± 15%	34% ± 13%	29% ± 14%	28% ± 13%
Time >250 mg/dL (%)	14% ± 10%	13% ± 9%	8% ± 7%	8% ± 7%
Mean Glucose (mg/dL)	172 ± 28	169 ± 24	159 ± 20	159 ± 20
Glucose SD (mg/dL)	64 ± 16	64 ± 14	55 ± 12	53 ± 12
Glucose CV (%)	37% ± 6%	37% ± 5%	34% ± 5%	33% ± 4%
CGM Hyperglycemic Event Rate per Week[a]	2.1 ± 2.2	2.0 ± 1.8	1.2 ± 1.2	1.0 ± 1.1
Daytime (6:00 AM – 11:59 PM)				
Time in Range 70-180 mg/dL (%)	59% ± 15%	61% ± 13%	68% ± 14%	69% ± 13%
Time in Range 70-140 mg/dL (%)	36% ± 14%	37% ± 13%	42% ± 12%	44% ± 13%
Time >180 mg/dL (%)	40% ± 16%	38% ± 14%	31% ± 14%	29% ± 13%
Time >250 mg/dL (%)	16% ± 11%	15% ± 10%	8% ± 7%	8% ± 7%
Mean Glucose (mg/dL)	177 ± 29	174 ± 26	161 ± 21	160 ± 20
Glucose SD (mg/dL)	66 ± 16	66 ± 14	55 ± 11	54 ± 11
Glucose CV (%)	37% ± 5%	38% ± 5%	34% ± 5%	33% ± 4%

	Pediatrics (6-17 Years)		Adults (18+ Years)	
	Humalog Lead-In Period (N=109) Mean± SD	**Lyumjev Treatment Period (N=109) Mean± SD**	**Humalog Lead-In Period (N=70) Mean± SD**	**Lyumjev Treatment Period (N=70) Mean± SD**
CGM Hyperglycemic Event Rate per Week [a]	1.9 ± 2.1	1.8 ± 1.7	0.9 ± 1.1	0.8 ± 0.9
Nighttime (12:00 AM – 5:59 AM)				
Time in Range 70-180 mg/dL (%)	73% ± 18%	75% ± 14%	72% ± 17%	73% ± 16%
Time in Range 70-140 mg/dL (%)	47% ± 21%	50% ± 18%	47% ± 18%	48% ± 18%
Time >180 mg/dL (%)	26% ± 19%	24% ± 14%	26% ± 17%	26% ± 16%
Time >250 mg/dL (%)	9% ± 10%	8% ± 7%	8% ± 9%	7% ± 7%
Mean Glucose (mg/dL)	158 ± 30	155 ± 23	156 ± 25	156 ± 23
Glucose SD (mg/dL)	51 ± 19	53 ± 15	52 ± 17	50 ± 14
Glucose CV (%)	32% ± 8%	34% ± 6%	33% ± 8%	32% ± 6%
CGM Hyperglycemic Event Rate per Week[a]	0.4 ± 0.6	0.4 ± 0.4	0.3 ± 0.6	0.3 ± 0.5

[a] Analytic definition of a CGM-Measured Hyperglycemic Event: A hyperglycemic event > 300 mg/dL is defined as spending a cumulative 90 minutes or more > 300 mg/dL in a 120-minute window. The end of the hyperglycemic event was defined as a minimum of 15 consecutive minutes with a sensor glucose concentration <180 mg/dL. When a hyperglycemic event ended, the study participant became eligible for a new event.

The change in central lab HbA1c from the end of the Humalog lead-in period to the end of the Lyumjev treatment period is summarized by age group below.

	Pediatrics (6-17 Years)		Adults (18+ Years)	
	End of Humalog Lead-In Period (N=109) Mean± SD	**End of Lyumjev Treatment Period (N=109) Mean± SD**	**End of Humalog Lead-In Period (N=70) Mean± SD**	**End of Lyumjev Treatment Period (N=70) Mean± SD**
HbA1c (%)	7.2 ± 0.9	7.1 ± 0.8	6.9 ± 0.8	6.7 ± 0.7

Challenge Results

During this clinical study, participants completed one meal challenge in the Humalog Lead-in Period and three meal challenges in the Lyumjev Treatment Period. Participants were instructed

to consume at least 50 grams of carbohydrates and either no bolus, a half bolus, or a full bolus was delivered. There were no CGM-measured hypoglycemic events (defined as at least 15 consecutive minutes <54 mg/dL) in the first three hours after the challenge in either the Humalog or Lyumjev periods. For the no bolus challenge, there were no significant differences in hypoglycemic event rates or any CGM metrics between periods in the first 3 hours post-meal, 4-5 hours post-meal, or overnight periods. For the full bolus and half bolus meal challenges, the percentage of hypoglycemic events was low during each time period.

One exercise challenge was completed by participants during the Humalog lead-in period and three exercise challenges were completed during the Lyumjev treatment period. Exercise challenges were 2 hours with at least 1 hour of moderate intensity exercise (remainder could be lower intensity). One percent of participants during the Humalog period and 2%, 1%, and 0% of participants during the 3 Lyumjev exercise challenges had at least 1 CGM hypoglycemic event < 54 mg/dL in the first 2 hours after starting exercise.

Clinical Literature Review

Based on existing literature of clinical studies assessing the safety and effectiveness of Lyumjev insulin, Control-IQ technology, and Control-IQ+ technology, the sponsor provided a justification for extrapolating the results of the pivotal clinical study of Control-IQ+ with Lyumjev described above (which included persons with Type 1 Diabetes ages 6 years and older) to support that Lyumjev U-100 insulin can be safely used with Control-IQ+ technology by adults 18 years and older with Type 2 Diabetes and children 2-5 years old with Type 1 Diabetes. The justification provided supports the proposed extrapolation.

Predetermined Change Control Plan (PCCP)

A predetermined change control plan (PCCP) for implementing the proposed labeling modifications to the device User Guide and Quick Start Guide upon clearance of a compatible ACE pump was provided in this submission. The PCCP includes a description of the labeling modifications, a modification protocol, and an impact assessment, and was determined to be adequate to support and clearly specify expectations, requirements, and specifications for updating the subject device labeling upon the clearance of a compatible ACE pump. Control-IQ+ Technology, with the proposed updated labeling, must not be distributed until the pre-specified acceptance criteria in the PCCP are met. Following implementation, new users will receive the updated Quick Start Guide upon receipt of their corresponding device, and the updated User Guide will be available electronically, or physically upon request. Existing users will be notified via email about the additional insulin compatible with the device and will have the option to either electronically download the updated User Guide and Quick Start Guide or request a physical version.

VII Proposed Labeling:

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

VIII Conclusion:

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