510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K262576

B Applicant

Deka Research and Development Corp.

C Proprietary and Established Names

twiist Loop Algorithm

D Regulatory Information

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

E Purpose for Submission:

Modification to the DEKA Loop cleared under K234055 to add an indication for patients with Type 2 diabetes mellitus in persons age 18 and greater.

II Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The twiist Loop Algorithm is intended for use with compatible integrated continuous glucose monitors (iCGMs) and the twiist alternate controller enabled (ACE) insulin infusion pump to automatically increase, decrease, and suspend delivery of basal insulin based on iCGM readings and predicted glucose values. It can also recommend, and with the user's confirmation, control the delivery of correction boluses when glucose values are predicted to exceed user configurable thresholds.

The twiist Loop Algorithm is intended for the management of type 1 diabetes mellitus in persons six years of age and greater and for the management of type 2 diabetes mellitus in persons eighteen years of age and greater.

The twiist Loop Algorithm is intended for single-patient use and requires a prescription.

C Special Conditions for Use Statement(s):

Rx – For Prescription Use Only

The twiist automated insulin delivery system is not intended for anyone unable or unwilling to:

- Test blood glucose (BG) levels as recommended by their healthcare provider.
- Maintain sufficient diabetes selfcare skills.
- See their healthcare provider regularly.
- Demonstrate adequate carbohydrate-counting skills (preferred, not required).

The twiist AID System should not be prescribed to patients with vision, hearing, cognitive, or physical impairments that would affect their ability to use the twiist AID System.

It is not indicated for use by anyone who is pregnant, on dialysis, or critically ill. It is not known how different conditions or medications used in these scenarios may affect performance of the twiist AID system. CGM readings being used by the system may be inaccurate in these cases, meaning the twiist AID system will not have accurate information to use for dosage recommendations. This could result in over-delivery or under-delivery of insulin, which can lead to low or high glucose.

Do not use the twiist AID system if you have a condition which, in the opinion of your healthcare provider, would put you at risk. Examples of individuals who should not use the twiist AID system include those with uncontrolled thyroid disease, renal failure (e.g. dialysis or eGFR <30), hemophilia, or another major bleeding disorder, or unstable cardiovascular disease.

twiist Loop combined with GLP-1 agonists, SGLT-2 inhibitors, DPP-4 inhibitors or metformin has only been studied in people with Type 2 diabetes mellitus and has not been studied in people with Type 1 diabetes mellitus. The performance of twiist Loop in conjunction with these medications is unknown in the Type 1 patient population.

III Device Description

The candidate device is the twiist Loop Algorithm, an interoperable automated glycemic controller (iAGC). It is a modification to the indications for use of the previously cleared DEKA Loop (K234055) by adding an indication for patients with Type 2 diabetes mellitus in persons age 18 and greater. No changes were made to the iAGC software code cleared under K234055.

The candidate device is intended for use with compatible integrated continuous glucose monitors (iCGMs) and the twiist alternate controller enabled (ACE) insulin infusion pump. It is intended to automatically increase, decrease, and suspend delivery of basal insulin based on readings from an iCGM and predicted glucose values. It can recommend correction boluses when glucose values are predicted to exceed user configurable thresholds and upon the user's confirmation, control the delivery of correction boluses.

The candidate device utilizes a dosing algorithm design to predict future glucose levels and adjust the amount of insulin to be delivered to the patient. The algorithm consists of four components involved in the automation of basal insulin delivery: insulin effect, carbohydrate effect, glucose momentum effect, and retrospective correction effect. It also utilizes these components to make recommendations for correction and meal boluses.

IV Substantial Equivalence Information:

A Predicate Device Name(s):

DEKA Loop

B Predicate 510(k) Number(s):

K234055

C Comparison with Predicate(s):

Device & Predicate Device(s):	K262576	K234055
Device Trade Name	twiist Loop Algorithm	DEKA Loop
General Device Characteristic Similarities		
Intended Use/Indications For Use	The twiist Loop Algorithm is intended for use with compatible integrated continuous glucose monitors (iCGMs) and the twiist alternate controller enabled (ACE) insulin infusion pump to automatically increase, decrease, and suspend delivery of basal insulin based on iCGM readings and predicted glucose values. It can also recommend, and with the user's confirmation, control the delivery of correction boluses when glucose values are predicted to exceed user configurable thresholds. The twiist Loop Algorithm is intended for the management of type 1 diabetes mellitus in persons six years of age and greater and for the management of type 2 diabetes mellitus in persons eighteen years of age and greater.	Same

General Device Characteristic Differences		
Intended use population	T1D six years of age and greater and T2D eighteen years of age and greater.	T1D six years of age and greater.
Compatible iGCM	Eversense 365 and FreeStyle Libre 3 Plus	Dexcom G6

V Standards/Guidance Documents Referenced:

Special controls established under 21 CFR 862.1356 for interoperable automated glycemic controller.

VI Performance Characteristics:

A. Non-Clinical Performance

Non-clinical performance is leveraged from the predicate submission.

B. Clinical Studies:

Summary of Clinical Testing

A clinical study was performed to validate the twiist Loop Algorithm for use in persons 18 years of age and greater diagnosed with Type 2 diabetes. A summary of the clinical study is provided in the following table:

Study Feature	Description
Title	A Single-arm Trial with an Innovative Automated Insulin Delivery System for Type 2 Diabetes ("twiist-T2D")
Study Objective	• To evaluate the efficacy of the twiist system with respect to glycemic outcomes in adults with T2D • To evaluate the safety of the twiist system in adults with T2D • To assess the impact of use of the twiist system on patient satisfaction and other patient reported outcomes.
Study Design	The study was a single-arm, open-label, multicenter clinical study conducted in adults aged 18 years and greater with insulin-treated T2D. The study evaluated the safety, performance, and usability of the device over a 13-week treatment period. HbA1c was the primary efficacy endpoint. The study was comprised of a Feasibility Phase followed by a Main Phase under one protocol. An independent Data and Safety Monitoring Board (DSMB) conducted an interim safety evaluation.

Study Feature	Description
	Following DSMB confirmation that no protocol modifications were required, enrollment proceeded into the Main Phase. Participants in both phases were followed for 13 weeks under identical study procedures, and their data were pooled for the final analysis.
Investigational Device	The twiist Loop Algorithm included in the twiist AID system that also includes an insulin pump and an Abbott Libre 3+ sensor
Study site	Thirty (30) sites in the United States
Inclusion Criteria	1. Age ≥18 years at the time of screening 2. Clinical diagnosis of Type 2 Diabetes for at least 6 months 3. Using one of the following insulin regimens for at least 13 weeks prior to screening: • Basal-bolus insulin therapy with at least one daily rapid-acting injection • Open-loop insulin pump therapy • Premixed insulin with a rapid-acting component • Basal insulin without bolus insulin 4. If using non-insulin glucose-lowering medications (e.g., GLP-1 receptor agonists, SGLT-2 inhibitors), dose must have been stable for at least 4 weeks prior to screening with no planned changes during the study 5. Willing and able to use only insulin approved for use in the study pump 6. Ability to read and understand written English or another available language for the pump's user interface 7. Sufficient cognitive capacity to provide informed consent, as judged by the investigator 8. Capable of safely operating all study devices and adhering to the protocol 9. Willing to participate in meal and exercise challenges 10. Participants capable of becoming pregnant must have a negative pregnancy test and agree to use accepted contraceptive measures
Exclusion Criteria	1. Diagnosis of Type 1 Diabetes

Study Feature	Description
	2. Prior use of an FDA-approved or non-FDA approved closed-loop or hybrid closed-loop insulin delivery system within the past 3 months 3. Pregnancy or breastfeeding at time of screening, or planning to become pregnant during the next 4 months 4. Concomitant disease or condition that may compromise patient safety (e.g., cystic fibrosis, severe mental illness, eating disorder) 5. Current use of an implantable CGM sensor (e.g., Senseonics) 6. Current use of ≥500 mg of ascorbic acid (Vitamin C) 7. Presence of a hemoglobinopathy or other condition affecting HbA1c measurement 8. Immediate family member of study site personnel or employees of Sequel Med Tech, DEKA, or affiliated organizations 9. More than 2 severe hypoglycemic events requiring third-party help or hospitalization within the last 6 months 10. More than one DKA or HHS event within the last 6 months 11. Lack of reliable telephone or internet service 12. Known allergy to medical grade adhesives or skin condition precluding use of the study pump or CGM 13. Current participation in another diabetes-related interventional clinical trial 14. Anticipated travel or change of residency for more than 14 days at a time during the study 15. Feasibility Phase only: Clarke Hypoglycemia Awareness Survey score of ≥4
Study Population and Breakdown of Subjects	The study enrolled adults (≥18 years) with insulin-treated Type 2 Diabetes (T2D). A total of: • 340 participants were consented and screened • 307 participants initiated use of the twiist system • 284 participants were included in the primary analysis population

Study Feature	Description
	• 223 participants were included in the per-protocol population • 307 participants were included in the safety population
Protocol Overview	The study comprised a Feasibility Phase (target ~30 participants) followed by a Main Phase (target ~270 participants). An independent Data and Safety Monitoring Board (DSMB) conducted an interim safety evaluation after 32 Feasibility participants had initiated twiist and 22 Feasibility participants had completed ≥ 3 weeks of twiist use. Following DSMB confirmation that no protocol modifications were required, enrollment proceeded directly into the Main Phase. Participants in both phases were followed for 13 weeks under identical study procedures, and their data were pooled for the final analyses. Following informed consent and eligibility confirmation, participants completed a CGM run-in of 2-3 weeks (which could be skipped by current Libre 3 CGM users), during which they continued their personal insulin regimen. Eligible participants then attended a Baseline visit to initiate use of the twiist system. The initial correction range was based on the participant's mean glucose from the baseline CGM data collection. Subsequent adjustments followed protocol-specified criteria. Virtual visits (phone or video) occurred 2–3 days after twiist initiation, at 7 ± 2 days, 3 weeks ± 4 days, and 6 weeks ± 4 days; an in-clinic visit occurred at 13 weeks ± 4 days. Participants who discontinued twiist were asked to attend an in-clinic early termination visit. The primary efficacy endpoint was change in HbA1c from baseline to 13 weeks, measured by a central laboratory. Patient-reported outcomes were collected at screening and 13 weeks. Participants completed two standardized home meal challenges and three standardized home exercise challenges during the treatment period.
Endpoints	Primary Endpoint: Change in HbA1c from baseline to 13 weeks (central laboratory measurement) Key Secondary Endpoints (Hierarchical Testing Order) 1. CGM-measured % time in range 70–180 mg/dL 2. CGM-measured % time in tight range 70–140 mg/dL

Study Feature	Description
	3. CGM-measured % time <54 mg/dL 4. CGM-measured % time <70 mg/dL 5. CGM-measured mean glucose 6. CGM-measured % time >180 mg/dL 7. CGM-measured % time >250 mg/dL 8. CGM-measured % time <70 mg/dL 9. CGM-measured % time <54 mg/dL Exploratory Endpoints • Binary HbA1c thresholds (<7.0%, <7.5%, reduction ≥0.5%, reduction ≥1.0%) • Additional CGM metrics (% time >300 mg/dL, coefficient of variation, prolonged hyperglycemia event rate, hypoglycemia event rate) • Binary CGM responder metrics (TIR >70%, time >180 mg/dL <25%, etc.) • Total daily insulin dose and percentage delivered as basal • Body weight and BMI • Patient-reported outcomes (PROs)
Safety Endpoints	Key safety outcomes monitored throughout the study: • Severe hypoglycemia (SH) events • Diabetic Ketoacidosis (DKA) events • Hyperosmolar Hyperglycemic Syndrome (HHS) events • Other Serious Adverse Events (SAEs) • Adverse Device Effects (ADEs) • Unanticipated Adverse Device Effects (UADEs) • CGM-measured time <54 mg/dL • CGM-measured prolonged hyperglycemia event rate per week • CGM-measured hypoglycemia event rate per week

Study Feature	Description
Summary of Results	• Primary Efficacy Endpoint: The mean HbA1c decreased from 8.15% ± 1.48% at baseline to 7.40% ± 0.89% at 13 weeks. The mean change from baseline was -0.74% (95% CI -0.88 to - 0.61). • Key Secondary Endpoints: Mean time in range 70-180 mg/dL increased from 57% ± 26% at baseline to 72% ± 17% at 13 weeks. The mean change was 15% (95% CI 13% to 18%). • Key Safety Endpoints: No severe hypoglycemia events occurred. There was one DKA event and no device malfunction was identified.

Participant Demographics

	PARTICIPANTS WHO INITIATED TWIIST (N=307)
Age at enrollment (years)	
Mean ± SD	58 ± 13
Range	19 to 85
Age >50 years old *n (%)*	235 (77%)
Sex – Female *n (%)*	143 (47%)
Ethnicity *n (%)*	
Hispanic or Latino	41 (13%)
Not Hispanic or Latino	265 (86%)
Unknown/not reported	1 (<1%)
Race *n (%)*	
White	193 (63%)
Black/African American	78 (25%)
Asian	14 (5%)
Native Hawaiian/Other Pacific Islander	5 (2%)
American Indian/Alaskan Native	1 (<1%)
More than one race	8 (3%)
Unknown/not reported	8 (3%)
Education *n (%)*	
Less than high school	9 (3%)
High school graduate/diploma/GED	91 (30%)
Technical/vocational	25 (8%)
Associate degree (AA)	40 (13%)
College graduate (Bachelor's degree or equivalent)	92 (30%)
Advanced degree (e.g. Masters, PhD, MD)	37 (12%)
Unknown	1 (<1%)
Do not wish to provide	12 (4%)

	PARTICIPANTS WHO INITIATED TWIIST (N=307)
Annual income *n (%)*	
<$25,000	23 (7%)
$25,000-<$35,000	22 (7%)
$35,000-<$50,000	24 (8%)
$50,000-<$75,000	49 (16%)
$75,000-<$100,000	45 (15%)
$100,000-<$200,000	65 (21%)
$200,000 or more	19 (6%)
Unknown/not reported	13 (4%)
Do not wish to provide	47 (15%)
Insurance *n (%)*	
Private only	148 (48%)
Medicaid only	29 (9%)
Medicare only	52 (17%)
Private and government	34 (11%)
Other government	31 (10%)
No coverage	1 (<1%)

Participant Characteristics – T2D Diabetes by Age and Duration

	PARTICIPANTS WHO INITIATED TWIIST (N=307)
Age at diagnosis of diabetes (years)	
Mean ± SD	39 ± 12
Range	12 to 71
Diabetes duration at enrollment (years)	
<5 years *n (%)*	22 (7%)
5-<10 years *n (%)*	26 (8%)
10-<20 years *n (%)*	126 (41%)
≥20 years *n (%)*	133 (43%)
Mean ± SD	19 ± 10
Range	1 to 51
Central lab HbA1c at baseline	N=305
<7.0% *n (%)*	51 (17%)
7.0%-7.9% *n (%)*	112 (37%)
8.0%-8.9% *n (%)*	74 (24%)
9.0%-9.9% *n (%)*	34 (11%)
≥10.0% *n (%)*	34 (11%)

	PARTICIPANTS WHO INITIATED TWIIST (N=307)
Mean ± SD	8.2 ± 1.5
Range	5.2 to 15.5
C-peptide (nmol/L)	N=304
Mean ± SD	1.13 ± 0.84
Median (Q1, Q3)	0.95 (0.57, 1.46)
Range	<0.007 to 6.48
GAD antibodies *n (%)*	N=305
<5 IU/mL	283 (93%)
5-250 IU/mL	12 (4%)
>250 IU/mL	10 (3%)
Any prior automated insulin delivery (AID) use in the last 5 years *n (%)*	59 (19%)
Any prior non-automated insulin pump use in the last 5 years *n (%)*	10 (3%)
Insulin modality at baseline *n (%)*	
Pump	2 (<1%)
Basal-bolus injections or inhaled insulin	223 (73%)
Pre-mixed insulin with a rapid component	7 (2%)
Basal-insulin only	75 (24%)
Total daily insulin dose (TDD) at baseline	
Mean ± SD (units/kg/day)	0.76 ± 0.46
Mean ± SD (units/day)	77 ± 52
Range (units/day)	5 to 285
>100 units/day *n (%)*	81 (26%)
Meal bolus method *n (%)*	
Fixed dose	86 (28%)
Small/medium/large	28 (9%)
Carbohydrate counting	35 (11%)
Sliding scale	72 (23%)
Not applicable	77 (25%)
Other	9 (3%)
CGM use at screening *n (%)*	258 (84%)
CGM use duration *n (%)*	
Not applicable	49 (16%)
<3 months	19 (6%)
3 months-<1 year	32 (10%)

	PARTICIPANTS WHO INITIATED TWIIST (N=307)
≥1 year	207 (67%)
CGM device type *n (%)*	
None	49 (16%)
Abbott 14-Day	2 (<1%)
Abbott Libre 2	19 (6%)
Abbott Libre 3	138 (45%)
Dexcom G6	6 (2%)
Dexcom G7	93 (30%)
Use of non-insulin glucose-lowering medications at enrollment *n (%)*	
None	41 (13%)
Metformin only	30 (10%)
GLP-1ra without SGLT2i	102 (33%)
SGLT2i without GLP-1ra	45 (15%)
GLP-1ra and SGLT2i	70 (23%)
Other[a]	19 (6%)
BMI (kg/m^2)	
BMI ≥30 kg/m^2 *n (%)*	193 (63%)
Mean ± SD	34 ± 8
Range	18 to 61

[a]Other non-insulin glucose-lowering medications at enrollment include: sulfonylurea only (N=8), sulfonylurea and metformin (N=4), metformin and thiazolidinedione (N=3), DPP4 only (N=1), DPP4 and metformin (N=1), DPP4 and sulfonylurea (N=1), DPP4, metformin, and sulfonylurea (N=1).

Primary Endpoint Results

	BASELINE (N=284)[a]	13 WEEKS (N=284)[a]	CHANGE FROM BASELINE (N=284)[a]
	Mean ± SD	**Mean ± SD**	**Mean (95% CI)[b]**
HbA1c (%)	8.15 ± 1.48	7.40 ± 0.89	-0.74 (-0.88, -0.61)

[a]Per the statistical analysis plan, participants were required to have an available HbA1c measurement at baseline and 13 weeks to be included in the analysis of HbA1c.

Secondary CGM-Measured Outcomes

	BASELINE (N=304)[a]	13 WEEKS (N=306)[a]	CHANGE FROM BASELINE (N=307)[b]	
	Mean ± SD	**Mean ± SD**	**Mean (95% CI)**	**P-Value[b]**

CGM hours	332 ± 12	1935 ± 390	-	-
% time 70-180 mg/dL	57% ± 26%	72% ± 17%	15% (13%, 18%)	<0.001
% time 70-140 mg/dL	32% ± 22%	44% ± 20%	12% (10%, 14%)	<0.001
% time <54 mg/dL [c]	0.02% ± 0.08%	0.02% ± 0.04%	0.00% (-0.01%, 0.01%)	<0.001
% time <70 mg/dL [c]	0.64% ± 1.22%	0.35% ± 0.50%	-0.26% (-0.39%, -0.12%)	<0.001
Mean glucose (mg/dL)	183 ± 51	158 ± 26	-25 (-29, -20)	<0.001
% time >180 mg/dL	42% ± 26%	27% ± 17%	-15% (-17%, -13%)	<0.001
% time >250 mg/dL[c]	13.1% ± 19.1%	5.2% ± 6.7%	-7.2% (-8.9%, -5.6%)	<0.001
% time <70 mg/dL[c]	0.64% ± 1.22%	0.35% ± 0.50%	-0.26% (-0.39%, -0.12%)	<0.001
% time <54 mg/dL[c]	0.02% ± 0.08%	0.02% ± 0.04%	0.00% (-0.01%, 0.01%)	0.74

[a] Among the 307 participants who initiated the study pump, N=3 at baseline and N=1 at 13 weeks did not have any CGM data available. Summary statistics are based on observed data only.

[b] N=307 with multiple imputation used to handle the participants who were missing the endpoint at baseline or 13 weeks. Paired t-tests were used to compare the change from baseline to 13 weeks. If the change was not normally distributed, a generalized linear regression model with the t-distribution was used instead of a paired t-test.

[c] Skewed outcomes. Summary statistics were calculated from an intercept only model assuming a t-distribution with 10 degrees of freedom for the errors in order to down-weight outliers.

C. Other Supportive Device Performance Characteristics Data

Leveraged from the predicate submission: Software, Cybersecurity, and HF validation.

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.