510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K220916

B Applicant

Beta Bionics, Inc.

C Proprietary and Established Names

iLet® Dosing Decision Software

D Regulatory Information

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

E Purpose for Submission:

New device

II Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The iLet Dosing Decision Software is intended for use with compatible integrated continuous glucose monitors (iCGM) and alternate controller enabled (ACE) pumps. A self-monitoring of blood glucose (SMBG) meter may also be used for manual input of blood glucose values to continue insulin dosing for a limited period of time when input from the iCGM is temporarily not available.

The iLet Dosing Decision Software autonomously determines and commands an increase, decrease, maintenance, or suspension of all basal doses of insulin and autonomously determines

and commands correction doses of insulin based on input from an iCGM, and it autonomously determines and commands meal doses of insulin based on meal announcements.

iLet Dosing Decision Software is intended for the management of type 1 diabetes mellitus in people 6 years of age or older. iLet Dosing Decision Software is intended for single patient use and requires a prescription.

C Special Conditions for Use Statement(s):

Rx – For prescription use only.

Do not use the iLet Dosing Decision Software if you are unable or unwilling to test blood glucose (BG) levels with an SMBG meter when input from the iCGM is not available.

Do not use the iLet Dosing Decision Software if you are unable or unwilling to recognize and respond to iLet safety alerts.

Do not use the iLet System if you are taking hydroxyurea, also known as Hydrea. This medication is sometimes used in the treatment of blood disorders and some kinds of cancer. The use of hydroxyurea can result in falsely elevated sensor glucose readings. The iLet System relies on sensor glucose readings to adjust insulin, provide insulin doses, and provide high and low glucose alerts. If the iLet System receives sensor readings that are higher than actual glucose levels, it could result in missed hypoglycemia alerts and potential errors in diabetes management, such as too much insulin being delivered. Hydroxyurea can also result in errors when reviewing, analyzing, and interpreting historical patterns for assessing glucose control.

Do not use the iLet ACE Pump and Dosing Decision Software in people under 6 years of age. The iLet ACE Pump and Dosing Decision Software have not been studied in these populations.

Do not use the iLet Dosing Decision Software in people who are pregnant, on dialysis or critically ill. The iLet Dosing Decision Software has not been studied in these populations.

The system should NOT be used in hospitalized people as the safety of the technology has not been evaluated in this population.

The iLet Dosing Decision Software is only for use with insulin U-100 lispro (Humalog), insulin U-100 aspart (Novolog), or insulin U-100 aspart (Fiasp).

Do not use the iLet Dosing Decision Software with the U-100 Fiasp in individuals under 18 years of age. The iLet Dosing Decision Software has not been studied with the U-100 Fiasp in these populations.

The iLet Dosing Decision Software is only for use with the Dexcom G6 iCGM. When using the iLet device, wear an iCGM.

Remove the iLet device, steel infusion set, CGM sensor, and CGM transmitter before undergoing radiation therapy, Magnetic Resonance Imaging (MRI), Computed Tomography (CT) scan, or diathermy treatment procedures. Exposure of the iLet device, steel infusion set, CGM sensor, or CGM transmitter to any of these may damage them.

Do not expose your iLet device, steel infusion set, CGM transmitter, or CGM sensor to equipment used in procedures for Pacemaker/Automatic Implantable Cardioverter Defibrillator (AICD) placement or reprogramming, Cardiac Catheterization, or Nuclear Stress Test.

The iLet Go App is compatible with the iOS platform. The iLet Go App provides the ability to perform over-the-air updates and / or pull data from an iLet device to share with the Beta Bionics Cloud. The iLet Go App is not currently compatible with Android or other platforms.

If your CGM is offline for an extended period of time, dosing will stop and you should switch to alternative therapy until you are able to reconnect to a CGM sensor. A countdown timer will appear before dosing would stop.

III Device Description

The iLet Dosing Decision software is part of the iLet Bionic Pancreas and is intended for use by people with diabetes. The iLet Dosing Decision software works in conjunction with a compatible alternate controller enabled (ACE) pump. The iLet Dosing Decision Software requires initialization with the user's body mass (body weight), as well as meal announcements. When initiating a meal announcement with the iLet Dosing Decision Software, the user qualitatively approximates carbohydrate content (meal size) relative to the usual carbohydrate content for each of the three meal types (breakfast, lunch, or dinner). The iLet Dosing Decision Software autonomously determine the size of the insulin dose in response to a meal announcement by the user.

The iLet Dosing Decision software works to control glucose to a user-set glucose target of "lower" (110 mg/dL), "usual" (120 mg/dL), or "higher" (130 mg/dL) within the device settings. Users can also set glucose targets specific for sleep.

The iLet Dosing Decision software also includes a feature, called "BG-Run mode", which enables the device to continue insulin delivery in the event CGM-data is unavailable. Use of the feature, however, should be temporary and always for the shortest duration possible, with the goal to resume CGM-guided insulin dosing as soon as possible.

IV Substantial Equivalence Information:

A Predicate Device Name(s):

Control IQ-Technology

B Predicate 510(k) Number(s):

K200467

C Comparison with Predicate(s):

Device & Predicate Device(s):	K220916	K200467
Device Trade Name	iLet® Dosing Decision Software	Control-IQ Technology
General Device Characteristic Similarities		
Intended Use/Indications For Use	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, as well as command correction doses, based on glucose values.	Same
Age Range of Intended Users	6 years and older	Same
General Device Characteristic Differences		
Specific Drug/Biologic Use	U-100 insulins: NovoLog, Humalog, and Fiasp	U-100 insulins: NovoLog and Humalog

V Standards/Guidance Documents Referenced:

Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices: Guidance for Industry and FDA Staff

General Principles of Software Validation: Guidance for Industry and FDA Staff

Design Considerations and Pre-market Submission Recommendations for Interoperable Medical Devices: Guidance for Industry and Food and Drug Administration Staff

AAMI TIR36:2007 - Validation of software for regulated processes

AAMI/AAMI HE75:2009(R2018)- Human factors engineering - Design of medical devices

AAMI/IEC TIR62366-2:2016 -Medical Devices Part 2: Guidance on the Application of Usability Engineering to Medical Devices

IEC 62304:2006+A1:2015 -Medical device software - Software life-cycle processes

AAMI/IEC 62366-1:2015 -Medical devices – Application of usability engineering to medical devices

ISO 14155:2020 - Clinical investigation of medical devices for human subjects - Good clinical practice

VI Performance Characteristics:

A. Analytical Performance

For the purposes of analytical and clinical validation testing, the iLet Dosing Decision Software was installed on the iLet ACE pump (K223846), which was paired with the Dexcom G6 continuous glucose monitoring system (K223931). Details on the performance characteristics of these devices can be found in the public decision summaries for each device.

B. Other Supportive Instrument Performance Characteristics Data

1. Summary of Clinical Testing

The sponsor conducted a randomized-controlled, prospective, multicenter pivotal clinical trial consisting of 440 participants (275 subjects ≥ 18 years old, and 165 subjects 6-17 years old) with type 1 diabetes. Subjects are randomized into the Bionic Pancreas (BP) Group or the Usual Care (UC) Group to complete the 13-week study period. The sponsor also conducted an ancillary study in which the iLet system's functioning was based only on SMBG manual entry, and no CGM data was available to the system.

Study Feature	Description
Title	The Insulin-Only Bionic Pancreas Pivotal Trial: Testing the iLet in Adults and Children with Type 1 Diabetes
Study Design	Randomized, prospective, multicenter clinical trial
Number of Sites	16
Population	Adults and children who were diagnosed with type 1 diabetes and were using insulin for at least a year were eligible for the study.
Sample Size	440 participants (275 adults, 165 pediatrics)
Treatment Groups	**Pediatric (6-17 years old) Study:** Random assignment in a 2:1 ratio to the BP Group (with Novolog or Humalog, hereafter referred to as the iLet-N/H group, ~ 110 participants) or the UC Group (~55 participants) , such that a minimum of 100 in the BP group will complete the 13-week Randomized Controlled Trial (RCT). **Adult (≥18 years) Study:** Random assignment in a 2:2:1 ratio to the BP Group (with Novolog or Humalog, iLet-N/H, ~ 110 participants), the BP Fiasp Group (iLet-F, ~ 110 participants), or the UC Group (~55 participants), such that a minimum of 100 in each BP Group complete the 13-week RCT.
Study Duration	3 months for primary study
Protocol Overview/Synopsis	The 13-week, parallel-group, multi-center RCT Period is designed to compare the insulin-only iLet BP Group using insulin lispro, insulin aspart, or Fiasp (adults only); and a control group following standard care (SC Group). **Key Eligibility Criteria** *Inclusion* 1. Clinical diagnosis of T1D for at least one year and using insulin for at least 1 year 2. Diabetes managed using the same regimen (either pump or MDI, with or without CGM) for ≥ 3 months 3. Age ≥ 6 years old 4. If a GLP-1 agonist or pramlintide is being used, participant must be

Study Feature	Description
	willing to discontinue use while the iLet BP system is being used, including the randomized trial and extension study. *Exclusion* 1. Plan to change usual diabetes regimen in the next 3 months 2. Use of Apidra as the pre-study rapid-acting insulin analog and unwilling to switch to lispro or aspart for the duration of the study 3. Known hemoglobinopathy (sickle cell trait is not an exclusion) 4. History of cystic fibrosis, pancreatitis, or other pancreatic disease, including pancreatic tumor or insulinoma, or history of complete pancreatectomy 5. Current use of SGLT2 inhibitors or a sulfonylurea drug (use more than 3 months prior to enrollment is acceptable) 6. Pregnant, breast feeding, plan to become pregnant in the next 3 months, or sexually active without use of contraception 7. Renal failure on dialysis or with an eGFR <30mL/min *Primary Endpoints* 1. HbA1c at 13 weeks 2. CGM time < 54 mg/dl *Key Safety Outcomes* • severe hypoglycemia • diabetic ketoacidosis • other serious adverse events

Demographics

Adult Study	Standard Care (N = 54)	iLet-F (N = 114)	iLet-N/H (N = 107)
Age (years)			
Mean (SD)	*44 (16)*	*42 (16)*	*44 (15)*
18 to < 25	7 (13%)	21 (18%)	16 (15%)
25 to < 45	21 (39%)	46 (40%)	38 (36%)
45 to < 60	13 (24%)	29 (25%)	33 (31%)
≥ 60	13 (24%)	18 (16%)	20 (19%)
Range	18 to 79	18 to 83	18 to 73
Diabetes Duration (years)			
Mean (SD)	29 (14)	24 (14)	26 (14)
HbA1c Level at Randomization (%)*			
Mean (SD)	*7.6 (1.2)*	*7.8 (1.2)*	*7.6 (1.2)*
<7.0	18 (34%)	31 (27%)	37 (35%)
7.1-7.4	6 (11%)	17 (15%)	17 (16%)
7.5%-<9.5	26 (49%)	56 (50%)	46 (43%)
≥9.5	3 (6%)	9 (8%)	7 (7%)
Range	5.5 to 11.3	5.3 to 14.9	5.5 to 13.1
Sex – Female n (%)	26 (48%)	62 (54%)	52 (49%)
Race/Ethnicity Group n (%)			
White non-Hispanic	47 (87%)	98 (86%)	85 (79%)
Black non-Hispanic	2 (4%)	10 (9%)	14 (13%)
Hispanic or Latino	3 (6%)	6 (5%)	7 (7%)
Asian	1 (2%)	0 (0%)	0 (0%)
American Indian/Alaskan Native	1 (2%)	0 (0%)	0 (0%)
More than one race	0 (0%)	0 (0%)	1 (<1%)
Unknown	0 (0%)	0 (0%)	0 (0%)

Pediatric Study	Standard Care (N = 53)	iLet-N/H (N = 114)
Age (years)		
Mean (SD)	12 (3)	12 (3)
6 to <12	47 (42%)	47 (42%)
12 to <18	65 (58%)	65 (58%)
Range	6 to17	6 to17
Diabetes Duration (years)		
Mean (SD)	7 (4)	6 (4)

Range	1 to 15	1 to 16
HbA1c Level at Randomization (%)		
Mean (SD)	*7.8 (1.1)*	*8.1 (1.2)*
<7.0	12 (23%)	18 (16%)
7.1-7.4	19 (36%)	34 (30%)
7.5%-<9.5	15 (28%)	33 (29%)
≥9.5	7 (13%)	27 (24%)
Range	5.8 to 10.6	6.1 to 12.2
Sex – Female n (%)	15 (28%)	55 (49%)
Race/Ethnicity Group n (%)		
White non-Hispanic	36 (68%)	72 (64%)
Black non-Hispanic	3 (6%)	13 (12%)
Hispanic or Latino	8 (15%)	16 (14%)
Asian	2 (4%)	2 (2%)
American Indian/Alaskan Native	0 (0%)	1 (<1%)
More than one race	4 (8%)	6 (5%)
Unknown	0 (0%)	2 (2%)

Safety Results

	Adult (Age ≥ 18 yr)			**Pediatrics (Age < 18 yr)**	
	iLet – N/H (N=107)	**iLet – F (N=113)**	**Standard of Care (N=54)**	**iLet – N/H (N=112)**	**Standard of Care (N=53)**
Total Number of Adverse Events (AEs)	63	83	6	181	4
Severe Hypoglycemic (SH) Events					
Number of SH Events per Participant *n (%)*					
0	100 (93%)	111 (97%)	53 (98%)	109 (97%)	52 (98%)
1	7 (7%)	3 (3%)	0 (0%)	3 (3%)	1 (2%)
2	0 (0%)	0 (0%)	1 (2%)	0 (0%)	0 (0%)
Incidence Rate per 100 Person-Years	25.5	10.2	14.2	10.4	7.3
Diabetic Ketoacidosis (DKA) Events					
Number of OKA Events					

	Adult (Age ≥ 18 yr)			Pediatrics (Age < 18 yr)	
	iLet – N/H (N=107)	**iLet – F (N=113)**	**Standard of Care (N=54)**	**iLet – N/H (N=112)**	**Standard of Care (N=53)**
per Participant *n (%)*					
0	107 (100%)	112 (98%)	54 (100%)	112 (100%)	53 (100%)
1	0 (0%)	2 (2%)	0 (0%)	0 (0%)	0 (0%)
Incidence Rate per 100 Person-Years	0	6.8	0	0	0
Other Serious Adverse Events (SAEs)					
Number of SAEs per Participant *n (%)*					
0	106 (>99%)	114 (100%)	53 (98%)	110 (98%)	52 (98%)
1	1 (1%)	0 (0%)	1 (2%)	2 (2%)	1 (2%)
Incidence Rate per 100 Person-Years	3.6	0	7.1	6.9	7.3
Participants with Worsening of HbA1c from baseline to 13 weeks by >0.5%					
n (%)	4 (4%)	7 (6%)	4 (8%)	13 (12%)	4 (8%)
Other Adverse Events (*N Events / N Participants*)					
Hyperglycemia with or without Ketosis Related to Study Device	34 / 27	52 / 40	0 / 0	126 / 68	0 / 0
Hyperglycemia with or without Ketosis Not Related to Study Device	13 / 12	14 / 12	0 / 0	41 / 32	2 / 1
Non-Severe Hypoglycemia	1 / 1	0 / 0	0 / 0	1 / 1	0 / 0
Other Reportable Adverse Events	7 / 7	12 / 10	3 / 3	8 / 7	0 / 0

Observed Results

	Adult (Age ≥ 18 years)			Pediatric (Age < 18 years)	
	iLet – N/H (N=107)	**iLet – F (N=113)**	**Standard of Care (N=54)**	**iLet – N/H (N=112)**	**Standard of Care (N=53)**
% Time<54 mg/dL					
Baseline median (IQR)	0.21% (0.02%, 0.57%)	0.12% (0.02%, 0.68%)	0.11% (0.00%, 0.37%)	0.20% (0.03%, 0.59%)	0.22% (0.03%, 0.46%)
Week 13 median (IQR)	0.33% (0.14%, 0.52%)	0.00% (-0.07%, 0.05%)	_*	-0.04% (-0.13%, 0.03%) [0.24]	_*
% Time 70-180 mg/dL					
Baseline mean (SD)	56% (19%)	54% (18%)	53% (21%)	47% (17%)	48% (19%)
Week 13 mean (SD)	69% (8%	71% (8%)	58% (17%)	60% (8%)	50% (16%)
% Time 70-180 mg/dL					
Adjusted Group Difference over 13 weeks (95% CI) [p-value]	11% (8%, 13%) [<0.001]	14% (11%,17%) [<0.001]	_*	10% (7%, 13%) [<0.001]	_*
Mean CGM Glucose (mg/dL)					
Baseline mean (SD)	179 (41)	181 (34)	186 (42)	195 (39)	195 (42)
Week 13 mean (SD)	157 (12)	155 (11)	174 (30)	172 (14)	187 (34)
Adjusted Group Difference over 13 weeks (95% CI) [p-value]	-16 (-20, -11) [<0.001]	-18 (-22, -14) [<0.001]	_*	-15 (-21, -9) [<0.001]	_*
Change in HbA1c after 13 Weeks					
Baseline	7.6	7.8	7.6	8.1	7.8
Week 13	7.1	7.1	7.5	7.5	7.8

* no data available

BG-Run Mode

The sponsor conducted an ancillary study after the conclusion of the RTC to evaluate the safety of utilizing BG values obtained by fingerstick instead of CGM as input into the iLet System. Fifty-four subjects (43 adults and 11 pediatrics) participated in the ancillary-phase of the study. Median time using BG measurements as input for the iLet System was 49.5 hours, with all participants having at least 46.5 hours of continued BG-run mode use. Median number of BG measurements entered during the first 24 hours was 9 and during the second 24 hours was 10. There were no incidences of severe hypoglycemia, DKA, or other serious adverse events (SAEs). Results of the ancillary study indicated that the frequency of low-sensor glucose events during the BG-run period appeared similar to the pre-randomization period and the RCT period, and the frequency of high-sensor glucose events during the BG-run period appeared higher than in the RCT-period.

2. Human Factors Testing

Human factors validation tests were conducted with the iLet Dosing Decision Software installed on the iLet ACE insulin pump (K223846). The summative human factors validation study was performed with 60 total users (45 primary users and 15 secondary users). All study participants received training that was consistent with the training that patients would receive with the commercial product. Usability evaluations assessed comprehension and usability of the device for critical device tasks. Results of the study demonstrated that the device could be used safely by intended users in the intended use environment when used in combination with a digitally connected device.

3. Insulin Compatibility

The iLet Dosing Decision Software used with the iLet Bionic Pancreas System is designed to use rapid-acting U-100 insulins including: NovoLog® (insulin aspart), Humalog® (insulin lispro), and Fiasp® (insulin aspart). These insulins were used in the pivotal clinical study for this device and no other insulins have been tested for use with the device.

4. Data Logging

Software verification testing has demonstrated the device records timestamped critical events, including information related to its state, user inputs, and device settings, as required by the special controls.

5. Interoperability

A plan and approach for interoperability were provided according to the FDA Guidance "Design Considerations and Pre-market Submission Recommendations for Interoperable Medical Devices - Guidance for Industry and Food and Drug Administration Staff" (issued on September 6, 2017) and determined to be adequate to support and clearly specify expectations, requirements, and interface specifications to potential interoperable devices. In addition, the plans provided by the sponsor covered their approach to working with connected device companies regarding contractual issues, interfaces for data communication and exchange, and post-market reporting procedures and responsibilities (e.g., who is responsible for investigating and reporting complaints, malfunctions, and adverse events).

The sponsor additionally provided validated software protocols intended to ensure secure, accurate, and reliable communication with digital interfacing devices, as well as failsafe design features to mitigate the risks associated with interruption of communication with digitally connected devices. These protocols were reviewed and found to be adequate.

6. Cybersecurity

Detailed information on cybersecurity of the device was reviewed and found to be acceptable. The sponsor also provided a software bill of materials, which provided details on all software used in the device and the hardware platform that the device was installed on. This included all manufacturer-developed, commercially licensed, open source, and off-the-shelf software components (including firmware as relevant), along with an identification of the hardware runtime environment in which each resides, with relevant version and/or model information, as well as details on whether each component was actively supported by its manufacturer or legacy licensed.

7. Postmarket Surveillance Study

There is uncertainty remaining regarding the risk/benefit profile of the device when used in the broader intended use population. While the premarket clinical study provided to support the 510(k) showed some benefits, it was not adequately powered to assess differences in the rates of safety events (e.g., diabetic ketoacidosis and severe hypoglycemia). Accordingly, a postmarket surveillance study will be ordered by FDA to confirm understanding of safety.

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.