October 2, 2020

Cyberdyne Inc.
Yohei Suzuki
Head of Production Department
2-2-1 Gakuen-Minami
Tsukuba, Ibaraki 305-0818
Japan

Re: K201559
Trade/Device Name: HAL for Medical Use (Lower Limb type)
Regulation Number: 21 CFR 890.3480
Regulation Name: Powered Lower Extremity Exoskeleton
Regulatory Class: Class II
Product Code: PHL, HCC
Dated: June 1, 2020
Received: June 10, 2020

Dear Yohei Suzuki:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part

801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Heather Dean, PhD
Assistant Director, Acute Injury Devices
DHT5B: Division of Neuromodulation
and Physical Medicine Devices
OHT5: Office of Neurological
and Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K201559

Device Name
HAL for Medical Use (Lower Limb Type)

Indications for Use *(Describe)*
HAL for Medical Use (Lower Limb Type) orthotically fits to the lower limbs and trunk;
HAL is a gait training device intended to temporarily help improve ambulation upon completion of the HAL gait training intervention. HAL must be used with a Body Weight Support system. HAL is not intended for sports or stair climbing. HAL gait training is intended to be used in conjunction with regular physiotherapy.

The device is intended for individuals with:
- spinal cord injury at levels C4 to L5 (ASIA C, ASIA D) and T11 to L5 (ASIA A with Zones of Partial Preservation, ASIA B);
- post stroke paresis
- paraplegia due to progressive neuromuscular diseases (spinal muscular atrophy, spinal and bulbar muscular atrophy, amyotrophic lateral sclerosis, Charcot-Marie-Tooth disease, distal muscular dystrophy, inclusion body myositis, congenital myopathy, muscular dystrophy) who exhibit sufficient residual motor and movement-related functions of the hip and knee to trigger and control HAL

In preparation for HAL gait training, the controller can be used while the exoskeleton is not donned to provide biofeedback training through the visualization of surface electromyography bioelectrical signals recorded.

HAL is intended to be used inside medical facilities while under trained medical supervision in accordance with the user assessment and training certification program

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) Summary

510(k) Number: K201559

5.1 Applicant Information

Date Prepared:	June 4, 2020
Company Name and Address:	CYBERDYNE Inc. 2-2-1, Gakuen-Minami, Tsukuba, Ibaraki 305-0818 Japan
Contact Person:	Mr. Yohei Suzuki Head of Production Department Phone: +81-29-869-8453 FAX: +81-29-869-8443 Email: suzuki_yohei@cyberdyne.jp

5.2 Device Information

Device Name:	HAL for Medical Use (Lower Limb Type)
Common or Usual Name:	Powered Exoskeleton
Classification Name:	Powered Lower Extremity Exoskeleton (primary) Biofeedback Device (secondary)
Regulation Number:	21 CFR 890.3480 (primary) 21 CFR 882.5050 (secondary)
Device Class:	II
Product Code:	PHL
Secondary Product Code:	HCC

5.3 Legally Marketed Predicate Device

510(k) Number:	K171909
Primary Predicate	Primary
Applicant:	CYBERDYNE Inc.
Device Name:	HAL for Medical Use (Lower Limb Type)
Regulation Number:	21 CFR 890.3480
Product Code:	PHL, HCC
Device Class:	II

5.4 Device Description

HAL for Medical Use (Lower Limb Type) is a battery powered lower extremity exoskeleton that provides assistive torque at the knee and hip joints for gait training. HAL is comprised of a controller, a main unit, and sensor shoes. The device comes in 8 size variations (4

different leg lengths and 2 different hip widths) for each of the 3 configuration types (double-leg, right-leg, and left-leg) and weighs ~14 kg (30 lbs). The device uses legally marketed cutaneous electrodes (up to 18 electrodes) to record surface electromyography bioelectrical signals of the hip and knee extensor and flexor muscles when the device is used in Cybernic Voluntary Control (CVC) mode. This mode provides assistive torque at the corresponding joint (e.g., hip or knee) using surface electromyography bioelectrical signals that are processed using a propriety signal processing algorithm. The propriety processing algorithm allows the device to detect surface electromyography bioelectrical signals to control the HAL device in CVC mode and provide visualization of the surface electromyography bioelectrical signals during biofeedback training. The assistive torque can be adjusted using three parameters: sensitivity level, torque turner, and balance turner. The device can also provide two additional modes: Cybernic Autonomous Control (CAC) mode and Cybernic Impedance Control (CIC) mode. CAC mode provides assistive torque leg trajectories based on postural cues and sensor shoe measurements. CIC mode provides torque to compensate for frictional resistance of the motor based on joint motion. CIC mode does not provide torque assistance for dictating joint trajectories. A trained medical professional (i.e., physician, physical therapist, etc.) can configure, operate, and monitor the device during gait training to make adjustments as needed.

Patients must exhibit sufficient residual motor and movement-related functions of the hip and knee to trigger and control HAL. The patient must be supported by a Body Weight Support (BWS) system before donning the device and during device use. The BWS must not be detached from the patient before doffing this device. HAL is not intended to provide sit-stand or stand-sit movements. HAL is capable of gait speeds up to approximately 2 km/hour on level ground. HAL is not intended for sports or stairclimbing.

In preparation to using HAL, the controller can be used while the exoskeleton is not donned to provide biofeedback training through the visualization of surface electromyography bioelectrical signals recorded.

HAL is intended to be used in conjunction with regular physiotherapy. HAL is intended to be used inside a medical facility under the supervision of trained medical professionals who have successfully completed the HAL training program.

5.5 Indications for Use

HAL for Medical Use (Lower Limb Type) orthotically fits to the lower limbs and trunk;
HAL is a gait training device intended to temporarily help improve ambulation upon completion of the HAL gait training intervention. HAL must be used with a Body Weight Support system. HAL is not intended for sports or stair climbing. HAL gait training is intended to be used in conjunction with regular physiotherapy.

The device is intended for individuals with:
- spinal cord injury at levels C4 to L5 (ASIA C, ASIA D) and T11 to L5 (ASIA A with Zones of Partial Preservation, ASIA B);
- post stroke paresis
- paraplegia due to progressive neuromuscular diseases (spinal muscular atrophy, spinal and bulbar muscular atrophy, amyotrophic lateral sclerosis, Charcot-Marie-Tooth disease,

distal muscular dystrophy, inclusion body myositis, congenital myopathy, muscular dystrophy)
who exhibit sufficient residual motor and movement-related functions of the hip and knee to trigger and control HAL.

In preparation for HAL gait training, the controller can be used while the exoskeleton is not donned to provide biofeedback training through the visualization of surface electromyography bioelectrical signals recorded.

HAL is intended to be used inside medical facilities while under trained medical supervision in accordance with the user assessment and training certification program.

5.6 Non-Clinical Performance Data

The subject devices demonstrate conformance with the following recognized standards:

- AAMI/ANSI ES60601-1:2005/(R)2012 and A1:2012
- IEC 60601-1-2:2014
- IEC 60601-1-6:2010 and IEC62366:2014
- IEC 62133:2012, IEC 60335-1:2010, IEC 60335-2-29:2010 and ANSI/UL 1012:2010
- IEC 62304:2015

The subject device underwent bench testing as part of required performance verification and validation activities. Results show that the subject device has met pre-defined design and performance acceptance criteria. Results of all non-clinical testing support the safety and effectiveness of the subject devices.

Testing	Objective(s) and Study Design
Stopper Strength Test	<Objective(s)> To evaluate the durability of the mechanical stopper of the actuator that limits the maximum angle and verify that it endures the mechanical force that can be applied by the patient <Results> Conformance with acceptance criteria was maintained after 100 cycles. The mechanical stopper is expected to endure the impact in the joints.

Consecutive Landing Test	<Objective(s)> Test the durability of the mechanical and electrical systems of HAL against repeated impacts with the ground that occur while walking. Confirm whether missing parts, cracks/chips of the exterior, loosening of screws, abnormal noises, looseness, operational malfunctions, and loosening/detachment/deformation of the connectors do not occur after 5-years worth (service life of HAL) of consecutive impacts and vibrations. <Results> All 3 samples withstood 3,000,000 [cycles] of landing impact, and there were no missing parts, cracks/chips of the exterior, loosening of screws, abnormal noises, looseness, operational malfunctions, and loosening/detachment/deformation of the connectors. The assumed maximum steps of HAL is 1,000,000[cycles] so it is sufficiently durable.
Effective Output Test	<Objective(s)> This test consists of two tests, each with different objectives below: A. Effective torque test: To verify that the actuator meets specifications for effective output torque by measuring the effective output torque to the input (electrical current). B. Maximum angle velocity test: To verify that the maximum angular velocity, generated when maximum torque is output, is within the range of that tolerable by the human knee joint. <Results> A. Effective torque output test: The output was verified to meet the specification. It was also within the range required by risk management. B. Maximum angular velocity test: The angular velocity was verified to be within a range that the human body can tolerate.
Driving Parts Performance Test	<Objective> To Measure the actual torque output against the torque output intended by the control algorithm, and confirm that it meets the performance criteria. <Results> The test results show that the actual torque output compared to the torque output intended by the control algorithm falls within the criteria range, and the performance of the driving parts meets the expected results.
Joint angle measurement	<Objective> To test the accuracy of joint angle sensing. <Results> Accuracy of joint angle measurement was verified to meet specification.
Body trunk absolute angle measurement	<Objective> To test the accuracy of body trunk absolute angle sensing. <Results> The measurement results show that the body trunk absolute angle measurement of the device can sufficiently detect the stable posture in the forward/backward directions of the patient, thus ensuring the safety and effectiveness of the device.
Plantar load measurement	<Objective> To test the accuracy of plantar load measurement.

	<Results> The measurement results show that the plantar force measurement of the device can sufficiently detect the planting and lifting of the sole, to enable the device to determine what phase (swing/support) each leg is in, thus ensuring the safety and effectiveness of the device.
Surface Electromyography Bioelectrical signal measurment performance	<Objective> To test the accuracy of surface electromyography bioelectrical signal measurement performance. The tests included an assessment of input impedance, common-mode rejection ratio, and frequency characteristics. <Results> Accuracy for all measurements were verified to meet specifications.
Ankle Durability Test	<Objective> Test the durability of the mechanical systems of the ankle parts against repeated impacts in a twisting direction, simulating impacts applied to the parts during a turning movement. Confirm whether missing parts, cracks/chips of the exterior, loosening of screws, abnormal noises, looseness do not occur after 5-years worth (service life of HAL) of consecutive impacts. <Results> All 3 samples withstood 300,000 [times] of impact, and there were no missing parts, cracks/chips of the exterior, loosening of screws, abnormal noises, looseness. The ankle part of the device is sufficiently durable.

5.7 Clinical Performance Data

Clinical performance data were collected for each of the disease groups through literature search and data held by the manufacturer.

<Group a: spinal cord injury>

6 items were assessed for effectiveness and 8 were assessed for safety. Results related to effectiveness of the treatment is summarized in the table below in the form of a pre-post comparison of gait function. Measurements were conducting without wearing HAL.

					10MWT speed					6MWT distance				
FDA-ID	Title	Authors	n		Pre	Post	Difference	P-value	MCID	Pre	Post	Difference	P-value	MCID
I1	Voluntary driven exoskelete	Aach et al.	8		0.28 +- 0.28 m/s	0.50 +- 0.34 m/s	0.22 m/s	<0.05		70.1 +- 130 m	163.3 +- 160.6 m	93.2 m	N/A, n=3 only	
I3	Against the odds: what to e	Grasmucke et	55		70.45 +- 61.50 s	35.22 +- 30.80 s	35.23 s	<0.001		97.81 +- 95.80 m	146.34 +- 118.13 m	48.53 m	<0.001	Forrest et al. 2004
I7	HAL exoskeleton training ir	Sczesny-Kais	11		0.25 +- 0.05 m/s	0.5 +- 0.07 m/s	0.25 m/s	<0.001	Musselman et al. 2007	86 +- 20.86 m	149.73 +- 20.32 m	63.73 m	<0.001	
I8	Hybrid Assistive Limb Exos	Jansen et al.	21		61.17 +- 44.27 s	32.18 +- 25.53 s	28.99 s	<0.001		90.81 +- 110.18 m	149.76 +- 144.28 m	58.95 m	<0.001	
I9	Functional Outcome of Neu	Jansen et al.	8	group 1	28.61 +- 6.9 s	21.22 +- 6.6 s	7.39 s	N/A		126.75 +- 19.25 m	149.5 +- 9.41 m	22.75 m	N/A	0.1 m/s (36m)
				group 2	34.28 +- 18.2 s	34.61 +- 17.3 s	-0.33 s	N/A	0.06 m/s	200 +- 117.42 m	209.5 +- 123.5 m	9.5 m	N/A	
I10	Reshaping of Gait Coordina	Puentes et al.	12		Only described as figure Gains in 10MWT speed in all acute and chronic patients					-	-	-	-	

While most of these studies do not have a control, the study populations were mostly chronic SCI where it is widely accepted that spontaneous recovery no longer occurs. The subjects from these studies may be considered their own control, and any changes seen should be attributed to the treatment with the device. From these results we conclude that treatment with the device results in meaningful improvements for SCI patients in terms of walking ability.

<Group b: stroke>

14 items were assessed for effectiveness and 4 were assessed for safety. Results related to the effectiveness of the treatment is summarized in the table below in the form of a pre-post comparison of gait function. Measurements were conducting without wearing HAL. The

tables are categorized by post stroke stages of the patient in order to explain the influence of spontaneous recovery.
Overall, the findings from these studies suggest that HAL therapy is an effective method for improving ambulatory function in stroke.

[Chronic stage: 6 months post stroke or longer]

					10MWT speed					6MWT distance				
FDA-ID	Title	Authors	n		Pre	Post	Difference	P-value	MCID	Pre	Post	Difference	P-value	MCID
I4	Pilot study of locomotion im	Kawamoto et	16	All subjects	0.41 +- 0.26 m/s	0.45 +- 0.24 m/s	0.04 m/s	<0.05	No MCID for chronic stage	-	-	-	-	Tang et al. 2012 34.4m
				FAC 2 and 3	0.24 +- 0.16 m/s	0.30 +- 0.19 m/s	0.06 m/s	<0.05		-	-	-	-	
				FAC 4 and 5	0.60 +- 0.21 m/s	0.60 +- 0.19 m/s	0.00 m/s	not sig.		-	-	-	-	
I15	Feasibility and efficacy of H	Yoshimoto et	18	HAL group	0.39 +- 0.18 m/s	0.60 +- 0.25 m/s	0.21 m/s	<0.001		-	-	-	-	
				CPT group	0.44 +- 0.16 m/s	0..42 +- 0.46 m/s	-0.02 m/s	not sig.		-	-	-	-	
I19	Spatiotemporal gait charac	Tanaka et al.	11		0.52 +- 0.32 m/s	0.66 +- 0.42 m/s	0.14 m/s	<0.05		-	-	-	-	

					10MWT speed				6MWT distance (*2MWT distance)				
FDA-ID	Title	Authors	n		Pre	Post	Follow up 3mo.	P-value (Pre-F/U)	MCID	Pre	Post	Follow up 3mo.	P-value (Pre-F/U)	MCID
I20	A follow-up study of the eff	Tanaka et al.	9		0.55 +- 0.30 m/s	0.72 +- 0.42 m/s	0.67 +- 0.36 m/s	<0.01	No MCID for chronic stage	*62.7 +- 36.1 m	*79.8 +- 46.6 m	*72.8 +- 38.2 m	0.02	Tang 2012 34.4m
FDA-ID	Title	Authors	n		Baseline	Crossover	Post	P-value		Baseline	Crossover	Post	P-value	
I18	A Randomized and Control	Sczesny-Kais	18	HAL -> CPT	0.49 +- 0.21 m/s	0.56 +- 0.23 m/s	0.60 +- 0.22 m/s	not sig. comparing		169.33 +- 81.87 m	190.38 +- 87.98 m	203.25 +- 86.53 m	not sig. comparing	
				CPT -> HAL	0.64 +- 0.29 m/s	0.80 +- 0.26 m/s	0.73 +- 0.3 m/s	the two groups		242.50 +- 132.15 m	243.06 +- 102.62 m	236.78 +- 115.03 m	the two groups	

Three studies (I4, I19, I20) do not have a legitimate control, but because the study populations are chronic, the subjects were not expected to make any gains from natural recovery based on historical prognoses, making them their own control. The other two studies (I15, I18) included a control group, with I15 having a parallel design and I18 having a cross-over design.
Although the overall results from the cross-over study (I18) did not show significant differences between the HAL group and control group, when comparing both groups in the first treatment period as in a parallel design, significant treatment effect was seen only in the HAL group. All the other studies show additional improvement effects with HAL treatment.

[Acute/subacute stages (during recovery)]

					10MWT speed (*6 minute walking test speed)					6MWT distance (*2MWT distance)				
FDA-ID	Title	Authors	n		Pre	Post	Difference	P-value	MCID	Pre	Post	Difference	P-value	MCID
I5	Gait training early after stro	Nilsson et al.	8		111.5 s	30 s	81.5 s	N/A	Perera et al. 2006 0.14m/s Tilson et al. 2010 0.16m/s	-	-	-	-	Perera et al. 2006 50m
I12	Locomotion improvement u	Watanabe et a	22	HAL group	0.61 +- 0.43 m/s	0.85 +- 0.43 m/s	0.24 m/s	<0.05		97.7 +- 107.6 m	156.7 +- 137.9 m	59.0 m	<0.05	
				CPT group	0.49 +- 0.55 m/s	0.63 +- 0.50 m/s	0.14 m/s	not sig.		111.3 +- 138.2 m	134.5 +- 132.1 m	23.2 m	not sig.	
I14	Effectiveness of Acute Pha	Fukuda et al.	53	Brs I	-	-	-	-		-	-	-	-	
				Brs II	-	-	-	-		-	-	-	-	
				Brs III	0.2 +- 0.1 m/s	0.4 +- 0.1 m/s	0.2 m/s	not sig.		-	-	-	-	
				Brs IV	0.4 +- 0.2 m/s	0.4 +- 0.2 m/s	0.0 m/s	not sig.		-	-	-	-	
				Brs V	0.7 +- 0.3 m/s	0.8 +- 0.4 m/s	0.1 m/s	<0.05		-	-	-	-	
				Brs VI	0.5 +- 0.3 m/s	0.9 +- 0.3 m/s	0.4 m/s	<0.05		-	-	-	-	
I16	Lateral Symmetry of Syner	Tan et al.	8		14.36 +- 12 m/min	31.47 +-12.11 m/min	17.11 m/min	<0.05		-	-	-	-	
I17	Reshaping of Bilateral Gait	Puentes et al.	11		*16.45 +- 10.1 m/min	*31.4 +- 13.2 m/min	*14.95 m/min	<0.01		97.93 +- 66.1	217 +- 77.9	119.07 m	<0.01	

					10MWT speed				6MWT distance (*2MWT distance)				
	Title	Authors	n		Pre	Post	Follow up 12wk.	P-value	MCID	Pre	Post	Follow up 12wk.	P-value (Pre-F/U)	MCID
I11	Effects of gait training usin	Watanabe et a	24	HAL group	0.56 +- 0.43 m/s	0.85 +- 0.43 m/s	0.84 +- 0.51 m/s	not sig. comparing	Perera 2006 0.14m/s Tilson 2010 0.16m/s	92.4 +- 104.2 m	156.7 +- 137.8 m	166.7 +- 143.9 m	not sig. comparing	Perera 2006 50m
				CPT group	0.45 +- 0.53 m/s	0.61 +- 0.47 m/s	0.57 +- 0.41 m/s	the two groups		106.9 +- 132.6 m	140.8 +- 127.8 m	131.0 +- 117.6 m	the two groups	
I21	Acute stroke rehabilitation	Yokota et al.	37	HAL group	FMA, FIM and FAC data only					FMA, FIM and FAC data only				
				CPT group	FMA, FIM and FAC data only					FMA, FIM and FAC data only				

The literature on the acute/subacute population also can be grouped by studies that have a control group or not. Four studies (I5, I14, I16, I17) did not have a control group, and though ambulatory function trended upward, these studies are highly limited by the fact that Stroke patients are known to make significant gains naturally in the acute/subacute phase of recovery.
Three studies (I11, I12, I21) had a control and although neither the 10MWT nor 6MWT were measured in one study (I21), the findings from the other two studies (I11, I12) show significant improvements in the HAL group that were not seen in the control group.

[End of recovery stage (just after improvement ceases)]

					10MWT speed (*6 minute walking test speed)					6MWT distance (*2MWT distance)				
FDA-ID	Title	Authors	n		Pre	Post	Difference	P-value	MCID	Pre	Post	Difference	P-value	MCID
I6	Gait training with Hybrid As	Yoshikawa et	16	HAL group	49.8 +- 20.1 m/min	61.4 +- 26.6 m/min	11.6 +- 10.6 m/min	<0.05 comparing the two groups	Perera et al. 2006 0.14m/s	*78.9 +- 33.3 m	*100.1 +- 40.6 m	*21.1 +- 12.4 m	not sig. comparing the two groups	Perera et al. 2006 50m
				CPT group	47.9 +- 24.9 m/min	50.1 +- 25.0 m/min	2.2 +- 4.1 m/min			*69.7 +- 33.9 m	*80.1 +- 38.3 m	*10.4 +- 8.9 m		
I13	Gait training of subacute st	Mizukami et a	8		49.8 +- 20.10 m/min	61.4 +- 26.64 m/min	11.6 m/min	<0.05	Tilson et al. 2010 0.16m/s	*78.9 +- 33.26 m	*100.1 +- 40.58 m	*22.2 m	<0.01	

Recognizing the challenges of ruling out natural recovery effects, two studies (I6 and I13) approached the treatment timing differently. The authors decided to apply HAL therapy only after the patients stopped showing improvements in walking function from regular physical therapy alone. This approach essentially makes these subjects similar to chronic stroke patients. The I6 study is an addendum to the I13 study, adding a non-randomized control group for comparison.
An ANCOVA analysis with group as a factor and baseline as a covariate showed a significant difference between the HAL group and control group for the 10MWT speed. Although the difference was not statistically significant for the 2MWT distance, patients in the HAL group showed greater improvement.

<Group c: progressive neuromuscular disease (see IFU for specific disease names)>
1 item of literature was assessed for both effectiveness and safety. Results from a clinical trial and post market survey were also assessed for both effectiveness and safety.

Literature for this group is limited due to the rare nature of the diseases and only one published study was assessed. I33 is a case report of 3 patients with Limb Girdle Muscular Dystrophy. No numerical results were reported, but the figures indicate that the 10MWT speed, Timed Up and Go test, and 6MWT distance showed an improvement in all subjects at the end of the 24 sessions of HAL therapy. The improvements in 10MWT speed and Timed Up and Go test remained at the 6 week follow up as well, though the 6MWT distance did not.
Since the literature is limited, performance needs to be further evaluated for this group using data generated or held by the manufacturer.
An investigator-initiated randomized controlled crossover clinical study approved by the Ministry of Health, Labour and Welfare of Japan was conducted for this patient population, and the results were used to gain medical device approval in Japan. The study, ID'd as I22, compared HAL therapy to a conventional gait training program as the control in an AB/BA crossover protocol, where each group received 9 sessions of each treatment in 4 weeks separated by a 1 week washout period. A total of 24 subjects completed the protocol, and inclusion criteria was patients who have ambulatory dysfunction due to one of the 8 rare progressive neuromuscular disorders for this group c.
For the primary endpoint, the 2MWT, the treatment effect was −10.066±11.062 (mean ± SD, hereinafter the same) (P=0.0369), which confirmed the therapeutic efficacy of HAL.

Furthermore, after the device's approval in Japan, data from Post-Market Surveillance have been collected over four years. Though certain aspects of control over adherence to the protocol used by I23 had to be ceded due to the nature of real world data, patients received 9 sessions of HAL therapy for each cycle, and the data was organized accordingly. As of November 2019 a total of 207 patients have participated in the PMS. Results support previous findings from the clinical trial that the device can maintain or even improve physical functions of patients with progressive neuromuscular disease. Overall, there were three main findings related to effectiveness and safety:

1) Participants showed improvement in gait related outcome measures comparing pre-post intervention of the first cycle of treatment (9 sessions). The results are in line with the results obtained in the clinical trial, which the design of the survey was based on.
2) Even after 1.5 years from the measurement of baseline, with intermittent treatment cycles participants showed about +20% difference from the baseline function, despite the progressive nature of their disease.
3) Blood creatine kinase data was collected from a total of 100 participants and results show a decreasing trend when comparing pre-post HAL treatment measurements. The lack of rise in CK levels suggests that HAL treatment does not damage the muscles through overuse.

5.8 Comparisons

5.8.1 Comparison of Intended Use/Indications for Use

Indications for Use	
Subject Device	**Predicate Device**
HAL for Medical Use (Lower Limb Type)	**HAL for Medical Use (Lower Limb Type) (K171909)**
HAL for Medical Use (Lower Limb Type) orthotically fits to the lower limbs and trunk; HAL is a gait training device intended to temporarily help improve ambulation upon completion of the HAL gait training intervention. HAL must be used with a Body Weight Support system. HAL is not intended for sports or stair climbing. HAL gait training is intended to be used in conjunction with regular physiotherapy. The device is intended for individuals with: - spinal cord injury at levels C4 to L5 (ASIA C, ASIA D) and T11 to L5 (ASIA A with Zones of Partial Preservation, ASIA B); - post stroke paresis - paraplegia due to progressive neuromuscular diseases (spinal muscular atrophy, spinal and bulbar muscular atrophy, amyotrophic lateral sclerosis, Charcot-Marie-Tooth disease, distal muscular dystrophy, inclusion body myositis, congenital myopathy, muscular dystrophy) who exhibit sufficient residual motor and movement-related functions of the hip and knee to trigger and control HAL. In preparation for HAL gait training, the controller can be used while the exoskeleton is not donned to provide biofeedback training	HAL for Medical Use (Lower Limb Type) orthotically fits to the lower limbs and trunk; the device is intended for individuals with spinal cord injury at levels C4 to L5 (ASIA C, ASIA D) and T11 to L5 (ASIA A with Zones of Partial Preservation, ASIA B), who exhibit sufficient residual motor and movement-related functions of the hip and knee to trigger and control HAL. HAL is a gait training device intended to temporarily help improve ambulation upon completion of the HAL gait training intervention. HAL must be used with a Body Weight Support system. HAL is not intended for sports or stair climbing. HAL gait training is intended to be used in conjunction with regular physiotherapy. In preparation for HAL gait training, the controller can be used while the exoskeleton is not donned to provide biofeedback training through the visualization of surface electromyography bioelectrical signals recorded. HAL is intended to be used inside medical facilities while under trained medical

through the visualization of surface electromyography bioelectrical signals recorded. HAL is intended to be used inside medical facilities while under trained medical supervision in accordance with the user assessment and training certification program.	supervision in accordance with the user assessment and training certification program

5.8.2 Similarities and Differences of Intended Use/Indications for Use (IFU)

The subject device expands upon the Indication for Use of the predicate device with the addition of these two patient populations. The stroke population and rare progressive neuromuscular diseases, namely Amyotrophic Lateral Sclerosis, Spinal Muscular Atrophy, Spinal and Bulbar Muscular Atrophy, Charcot-Marie-Tooth Disease, Muscular Dystrophy, Distal Myopathy, Congenital Myopathy and Inclusion Body Myositis.

The inclusion of individuals with post stroke paresis is not uncommon among the devices in the 21 CFR 890.3480 regulation. Individuals with progressive neuromuscular diseases is a new population not found in the indications of any marketed device. Moreover there are not many medical services available for this population, with the exception of several pharmaceuticals.

The new additions to the target patient population raise different questions of safety and effectiveness, but the additional clinical evidence presented show that the device is both safe and effective for these populations.

5.8.3 Comparison of Characteristics

Device	Subject Device (HAL for Medical Use)	Predicate Device (HAL for Medical Use K171909)
Limitations	• Healthy bone density. • Skeleton does not suffer from any fractures. • In general good health. • Candidates of the device should have the following characteristics: • i. Hip width and leg segment lengths are within the range of adjustability • ii. Weight is within the range of 40 - 100 kg (89 - 220 lbs) • iii. Height is within the range of 150-190 cm (60 ~ 74 in), with allowance for exceptions as long as the leg segment length is within the range of adjustability Judgment of whether this device is	• Healthy bone density. • Skeleton does not suffer from any fractures. • In general good health. • Candidates of the device should have the following characteristics: • i. Hip width and leg segment lengths are within the range of adjustability • ii. Weight is within the range of 40 - 100 kg (89 - 220 lbs) • iii. Height is within the range of 150- 190 cm (60 ~ 74 in), with allowance for exceptions as long as the leg segment length is within the range of adjustability Judgment of whether this device is

Device	Subject Device (HAL for Medical Use)	Predicate Device (HAL for Medical Use K171909)
	suitable for a person with an unusual body shape (such as deformation of the leg) shall be made after comprehensive consideration of leg length, hip width, positions of cuffs and belts, sizes of sensor shoes, and fit of the joint positions and frame to the person's body. • Physical and cognitive ability to use a treadmill, walker, or parallel bars. Use does not need to be independent of clinical support. • Ability to communicate pain and need to cease session, verbally or nonverbally. • Ability to acknowledge communication from the therapist, verbally or nonverbally.	suitable for a person with an unusual body shape (such as deformation of the leg) shall be made after comprehensive consideration of leg length, hip width, positions of cuffs and belts, sizes of sensor shoes, and fit of the joint positions and frame to the person's body.
Contraindications	• Persons whose body dimensions such as weight, upper leg length, lower leg length and hip width, are not suitable for this device. • Persons who have severe deformations of their body parts.* • Persons whom physicians have judged unsuitable for the implementation of therapeutic exercise such as standing and walking treatment. • Persons who cannot have electrodes affixed to any part of their body due to a skin disease or any other reason. • Severe spasticity (Ashworth4) • Unstable spine or unhealed limbs or pelvic fractures. • Heterotopic ossification. • Significant contractures. • Psychiatric or cognitive situations that may interfere with proper operation of the device. • Cognitive impairments resulting in	• Persons whose body dimensions such as weight, upper leg length, lower leg length and hip width, are not suitable for this device. • Persons who have severe deformations of their body parts.* • Persons whom physicians have judged unsuitable for the implementation of therapeutic exercise such as standing and walking treatment. • Persons who cannot have electrodes affixed to any part of their body due to a skin disease or any other reason. • Severe spasticity (Ashworth4) • Unstable spine or unhealed limbs or pelvic fractures. • Heterotopic ossification. • Significant contractures. • Psychiatric or cognitive situations that may interfere with proper operation of the device. • Pregnant women. • History of severe neurological

Device	Subject Device (HAL for Medical Use)	Predicate Device (HAL for Medical Use K171909)
	inability to follow directions. • Pregnant women. • History of severe neurological injuries other than SCI, stroke, spinal muscular atrophy, spinal and bulbar muscular atrophy, amyotrophic lateral sclerosis, Charcot-Marie-Tooth disease, distal muscular dystrophy, inclusion body myositis, congenital myopathy or muscular dystrophy (MS, CP, TBI, subarachnoid hemorrhage, etc.) • Persons with severe concurrent medical diseases: infections, circulatory, heart or lung, pressure sores • Persons with colostomy • Persons with poor skin integrity in areas in contact with the device • Persons with decreased standing tolerance due to orthostatic hypotension • Persons with strict range of motion (ROM) restrictions that cannot tolerate the entire ROM of HAL, or that would prevent a patient from achieving a normal, reciprocal gait pattern • Persons with unresolved deep vein thrombosis • Persons with uncontrolled Autonomic Dysreflexia • Persons with uncontrolled hypertension or hypotension • Persons with lower limb prosthesis • Persons who require ventilators • Persons with epilepsy	injuries other than SCI (MS, CP, ALS, TBI, etc.) • Persons with severe concurrent medical diseases: infections, circulatory, heart or lung, pressure sores • Persons with colostomy • Persons with poor skin integrity in areas in contact with the device • Persons with decreased standing tolerance due to orthostatic hypotension • Persons with strict range of motion (ROM) restrictions that cannot tolerate the entire ROM of HAL, or that would prevent a patient from achieving a normal, reciprocal gait pattern • Persons with unresolved deep vein thrombosis • Persons with uncontrolled Autonomic Dysreflexia • Persons with uncontrolled hypertension or hypotension • Persons with lower limb prosthesis • Persons who require ventilators • Persons with epilepsy
Patient Height	Same	150-190 cm
Patient Weight	Same	40-100 kg
Intended Environment	Same	• Flat surface of training/rehabilitation facility (indoor only) • Must be used in combination with

Device	Subject Device (HAL for Medical Use)	Predicate Device (HAL for Medical Use K171909)
		Body Weight Support systems
Intended Users	Same	Medical professionals that have completed designated training program to use the device
Hardware and Main Components	Same	The system consists of three major components: • Controller • Main unit • Sensor shoes
Device Variations	• Double leg configuration and Single leg configurations (right and left configurations) • Same • Same	• Double leg configuration • 8 different size variations: 4 different leg lengths, 2 different waist widths • Sensor shoes are available in different sizes of 23, 24, 25, 26, 27, 28, 29, 30 cm
Device Lifetime	Same	5 Years
Power Sources	Same	• Lithium ion battery
Range of Motion	Same	• Hips: 120° flexion to -20° extension • Knee: 120° flexion to -6° extension
Method of Control	Same	• Surface electromyography Bioelectrical signals at knee and hip extensor and flexor muscles (CVC mode), Attached controller used by medical professional, Postural and Shoe sensor cues for movement
Modes of Operation	Same	• CVC (Cybernic Voluntary Control) • CAC (Cybernic Autonomous Control) • CIC (Cybernic Impedance Control) *Can be selected for each joint (right/left hip/knee joints)
Main risk (mitigation)	Same	Drive patient's joints past their ROM (mechanical stoppers)
Safety Features	Same	• Limited joint torque and joint velocity • Mechanical stoppers to prevent excessive joint flexion or extension • System fault for each component throughout operation • Task switching conditions that will

Device	Subject Device (HAL for Medical Use)	Predicate Device (HAL for Medical Use K171909)
		not initiate incorrect task changes
Fall Prevention Measures	Same	BWS systems
Bench Testing	Same	• Durability of mechanical stopper: applicant test • Durability of ankle part Consecutive Landing: applicant test • Effective output: applicant test • Software testing: Verification, validation & hazard analysis
Operating Temperature	Same	• 50° to 86° F (10° to 30° C)
Performance Standards	• Same • Electromagnetic Compatibility: IEC 60601-1-2 Edition 4.0, 2014 • Same • Same • Same	• Electrical Safety: AAMI/ANSI ES60601-1:2005/(R)2012 and A1:2012 • Electromagnetic Compatibility: IEC 60601-1-2: 2007 • Usability: IEC 60601-1-6: 2010 and IEC 62366: 2014 • Battery Safety: IEC 62133: 2012, IEC 60335-1: 2010, IEC 60335-2-29: 2010 and ANSI/UL 1012: 2010 • Software: IEC 62304: 2015
Training	Same (training material has been updated to address new indications and description of additional configurations)	• CYBERDYNE-developed program for medical professionals • The device is intended to be used only in medical facilities for HAL gait training • Must be used under the supervision of a trained medical professional in accordance with the user assessment and training certification program.
Clinical Studies	<Group a: spinal cord injury> • There are 6 studies conducted on spinal cord injury subjects, that include the 2 studies listed in K171909, used for assessment of effectiveness. There are 8 studies that were used for assessment of safety. • All studies were non-comparative and non-randomized. One study with an ID of I9 had 2 groups with	• There are 2 studies conducted on spinal cord injury subjects. The studies cover the indications for use of the device. Both effectiveness and safety are measured in the studies and statistical analysis has been performed for results on effectiveness. • The studies were both non-comparative and non-randomized.

Device	Subject Device (HAL for Medical Use)	Predicate Device (HAL for Medical Use K171909)
	different treatment frequencies. • Subjects were mostly chronic SCI patients with the same range of lesion as the studies in K171909. • The sample size range of the studies are the same, 8 ~ 55. • Results on effectiveness of 3 of the newly added studies are consistent with the findings from K171909. The 4th newly added study, I9, showed that gains made from treatment with the HAL device were maintained for a year with continued treatment at the same treatment frequency as during the intervention, as well as with continued treatment at a much lower frequency. • Results on safety is the same, that there were no SAEs reported, and all adverse events were minor incidents. Adverse events that occurred with use of other devices is unlikely to occur with the use of the HAL because falls are mitigated with a mandatory combined use with a BWS system, use on patients with low bone density is labeled as a limitation, and a swollen ankle has never been reported in our global market experience. It is assumed that the sensor shoes, which is an essential component of the HAL, protects the ankle from making physical contact with the rigid parts of the device. • Long term use of the device has been tested, and the result supports long term effects of treatment even with decreased treatment frequency. <Group b: stroke> • There are 14 studies conducted on stroke subjects used for assessment of effectiveness. Of these, 5 were studies for patients of over 6 months	• All subjects were chronic (> 1 year since trauma) SCI patients with injuries ranging from C2-L5, ASIA D, C, B and ASIA A with Zones of Partial Preservation • The sample size of the studies are 8 and 55 subjects, respectively • The effectiveness is primarily measured by 10 meter walk tests, 6 minute walk tests, and WISCI-II tests, all measured without wearing the HAL device. The results suggest a statistically significant improvement in gait related outcome measures. • The safety of the device is primarily measured by SAE and AE occurrences. There were no SAE reported. AE's included reports of minor incidents that included: pain due to pressure from device parts that were managed by adjusting a better fit, skin irritation from electrodes and chafed feet due to wrong shoe size. • Long term use of over 12 weeks (60 treatment sessions) has not been clinically tested.

Device	Subject Device (HAL for Medical Use)	Predicate Device (HAL for Medical Use K171909)
	post stroke and 7 were for patients of less than 6 months post stroke. The remaining 2 studies monitored weekly 10MWT results during conventional physical therapy/rehabilitation after stroke, and started the intervention with HAL when the walk speeds stopped showing improvements. There are 4 studies that were used for assessment of safety. • Some studies were comparative with a control group receiving conventional physical therapy. • The sample size range of the studies are 8 ~ 53. • The effectiveness is primarily measured by the 10MWT and 6MWT, all measured without wearing the HAL device. Overall, the results suggest a statistically significant improvement in gait related outcome measures. Results from studies that could not rule out the effects of spontaneous recovery early after the onset of stroke still trended toward improvement of gait related outcome measures, and the studies that addressed spontaneous recovery, either through intervention timing or with a control group, suggest that the treatment with the device show statistically and clinically significant improvements in gait related outcome measures while conventional physical therapy does not. • The safety of the device is primarily measured by SAE and AE occurrences. Results on safety suggest that there are no adverse events typical of the disease. No SAEs are reported. • Though limited, there are some studies that support either lasting or long term effects.	

Device	Subject Device (HAL for Medical Use)	Predicate Device (HAL for Medical Use K171909)
	<Group c: neuromuscular disease> • There are 3 studies (1 literature, 1 clinical trial and 1 post market survey) conducted on patients with diseases belonging in the group. All 3 studies account for both safety and effectiveness. • The sample size range of the studies are 3 ~ 207. • The effectiveness is primarily measured by the 10MWT and 2MWT, all measured without wearing the HAL device. Results suggest that treatment with the HAL device shows improvement in gait related outcome measures despite the progressive nature of the diseases. Since the literature and clinical trial have such small sample sizes, the findings from the post market survey bears significant weight and are quickly summarized below: 1) Participants showed improvement in gait related outcome measures comparing pre-post intervention of the first cycle of treatment (9 sessions). 2) Even after 1.5 years from the measurement of baseline, with intermittent treatment cycles participants showed about +20% difference from the baseline function, despite the progressive nature of their disease. 3) Blood creatine kinase data was collected from a total of 100 participants and results show a decreasing trend when comparing pre-post HAL treatment measurements. The lack of rise in CK levels suggests that HAL treatment does not damage the muscles through overuse.	

Device	Subject Device (HAL for Medical Use)	Predicate Device (HAL for Medical Use K171909)
	• The safety of the device is primarily measured by SAE occurrences. No device caused SAEs are reported. • Long term effects are evident from post market survey results.	
Special Controls	Same	Conforms with special controls per 21 CFR 890.3480, as applicable

5.8.4 Similarities and Differences of Non-clinical Performance Data

The subject device is an expansion of the predicate device, so the characteristics that they share are many and exactly the same.

The contraindications were adjusted slightly to reflect the addition of stroke and progressive neuromuscular diseases in the indication, as well as to reflect the exclusionary criteria from the studies used to show safety and effectiveness for these new populations.

The subject device adds two single-leg configurations; right and left leg configurations. Each of these additional configurations come with all of the size/shape variations of the double leg device, as well as the different Sensor Shoe sizes. The difference between the single-leg versions and the double-leg version is simple. One of the legs, from the hip joint down has been removed from the main unit, and it is replaced by a long cord that attaches to one of the sensor shoes. The sensor shoe still provides floor reaction force sensor readings, but no assistance is provided for the side with no device leg.

Though different questions about safety may seem like to arise due to the difference in configurations, the non-clinical performance testing also applies to the new single-leg versions. Safety is therefore not compromised.

5.8.5 Similarities and Differences of Clinical Performance Data

<Spinal Cord Injury>
In addition to the clinical studies presented for the predicate device that demonstrated safety and efficacy for spinal cord injury, the additional studies presented for the subject device increases the robustness of evidence supporting safety and efficacy.

<Stroke>
Stroke is a new indication. Safety and effectiveness for this population is supported by many

clinical studies, although the significance level of the changes in outcome measures that show effectiveness vary among the studies.

The most representative finding comes from a comparative clinical study for 16 post stroke subjects (8 with HAL and 8 with conventional gait rehabilitation). All subjects were new stroke survivors who underwent conventional rehabilitation until their gait function ceased to improve, showing the end of natural recovery as well as the limits of the effects of conventional rehabilitation. This timing was determined through monitoring of weekly measurements of the 10 meter walk speed. Once gait function ceased to improve from conventional rehabilitation, subjects started the comparative intervention, and results after a 5 week treatment program (5 sessions per week) were compared to show significant differences between the two groups. The group that used the HAL showed great additional improvement (greater than the MCID) whereas the group that continued conventional gait rehabilitation did not show much change. The results of the control group indirectly proves that the criteria used to identify the “end” of natural recovery & rehabilitation was valid, which in turn suggests that the treatment with HAL provides additional improvements for patients in this population.

<Progressive Neuromuscular Diseases>
Patients with progressive neuromuscular disease are not the typical population to use this type of medical device. However a GCP clinical trial and post market survey in Japan shows temporary effects for this population. Although the speed of disease progression greatly depends on the type of disease and the progression phase, as a group, treatment with the HAL helped patients maintain their physical function (distance walked in 2 minutes) above the baseline level before starting treatment for over 1.5 years. Also noteworthy was the finding that CK (Creatine Kinase) levels did not elevate after treatment and instead showed a slight tendency to decrease, which suggests that treatment with HAL does not lead to overuse or excessively burden the muscles when used for patients in this population.

5.9 Conclusions

Based on the information above with comparisons of intended use, indications for use, and technological characteristics, the new differences that raise different questions of safety and effectiveness were addressed, and we believe that the subject device is as safe and effective as, and therefore substantially equivalent to, the identified predicate device.