DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

June16, 2017

BIOHERMES CO., LTD
C/O FIELD FU, SHENZHEN JOYANTECH CONSULTING CO., LTD.
ROOM 2032, INTERNATIONAL MAYORS COMMUNICATION CENTRE,
NO. 55 SHIZHOU MIDDLE ROAD, NANSHAN DISTRICT
SHENZHEN, GD755 CHINA

Re: K161533
Trade/Device Name: A1C EZ Glycohemoglobin Analysis System
Regulation Number: 21 CFR 864.7470
Regulation Name: Glycosylated hemoglobin assay
Regulatory Class: II
Product Code: LCP, JJE
Dated: May 3, 2017
Received: May 8, 2017

Dear Field Fu:

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. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Kellie B. Kelm -S

for Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k161533

Device Name
A1C EZ Glycohemoglobin Analysis System

Indications for Use *(Describe)*
A1C EZ Glycohemoglobin Analysis System is an in vitro diagnostic test used to quantitatively measure the percent glycohemoglobin A1c or glycohemoglobin A1c fraction mmol/mol in venous whole blood samples. This system is intended for multiple patient use to monitor long term glycemic control in individuals previously diagnosed with diabetes. This test is not to be used for screening or diagnosis of diabetes or for neonatal use. The A1C EZ Glycohemoglobin Analysis System is intended for professional use in clinical laboratories only.

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.

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K161533

510(k) Summary

1. Contact Details

1.1 Applicant information

Applicant Name	BioHermes Co., Ltd
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Contact person	Rao Qiangying
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Date Prepared	March 28, 2016
Website	www.biohermes.com

1.2 Submission Correspondent

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Phone No.	+86-755-86069197
Contact person	Christy Young; Field Fu;
Contact person's e-mail	christy@cefda.com; cefda13485@163.com;
Website	http://www.cefda.com

2. Device information

Trade name	A1C EZ Glycohemoglobin Analysis System
Common name	Percent Hemoglobin A1c (percent glycosylated hemoglobin)
Model	/
Classification	II; I
Classification name	Assay, Glycosylated Hemoglobin; Analyzer, Chemistry (Photometric, Discrete), For Clinical Use
Product code	LCP; JJE
Regulation No.	864.7470;862.2160

3. Legally Marketed Predicate Device

Trade Name	A1CNow+ (Professional Use)
510(k) Number	K090413
Product Code	LCP
Manufacturer	Bayer HealthCare Diabetes Care

4. Device Description

This product is used to quantitatively measure the percent glycohemoglobin A1c or glycohemoglobin A1c fraction mmol/mol in human whole blood sample.

5. Intended Use/Indication for Use

A1C EZ Glycohemoglobin Analysis System is an in vitro diagnostic test used to quantitatively measure the percent glycohemoglobin A1c or glycohemoglobin A1c fraction mmol/mol in venous whole blood samples. This system is intended for multiple patient use to monitor long term glycemic control in individuals previously diagnosed with diabetes. This test is not, to be used for screening or diagnosis of diabetes or for neonatal use. The A1C EZ Glycohemoglobin Analysis System is intended for professional use in clinical laboratories only.

6. Substantial Equivalence Comparison

Item	**Proposed Device: A1C EZ Glycohemoglobin Analysis System**	**Predicate Device: A1CNow+ (Professional Use) (K090413)**
Product Code	LCP,JJE	LCP
Intended Use	A1C EZ Glycohemoglobin Analysis System is an in vitro diagnostic test used to quantitatively measure the percent glycohemoglobin A1c or glycohemoglobin A1c fraction mmol/mol in venous whole blood samples. This system is intended for multiple patient use to monitor long term glycemic control in individuals previously diagnosed with diabetes. This test is not to be used for screening or diagnosis of diabetes or for neonatal use. The A1C EZ Glycohemoglobin Analysis System is intended for professional use in clinical laboratories only.	The A1CNow multi-use test provides quantitative measurement of the percent of glycated hemoglobin (%HbAlc, %A1C) levels in whole blood samples. The test is for professional use for monitoring glycemic control in people with diabetes.
Sample Types	Whole blood sample	Whole blood samples
Calibration	Automatic, not required by end-user	Not required by end-user; each unit is factory calibrated
Testing Environment	Professional Use	Professional Use
Room Temperature Stability	18 months room temperature	15 months room temperature
Methodology	Boronate Affinity	Immunoassay
Measuring Range	4%-14% HbA1c	4%-13% HbA1c

<table>
<tr><td>Precision</td><td>The overall imprecision (including within-run, between-run, and between-day) was 3.3% CV at the low level and 2.8% CV at the high level.</td><td>The overall imprecision (including within-day and between day) was 3.00% CV at the low level and 4.02% CV at the high level.</td></tr>
<tr><td>Accuracy</td><td>Linear regression analysis of comparison study between A1c EZ 2.0 and Tosoh G8
<table><tr><td></td><td>Slop</td><td>Intercept</td></tr><tr><td>Lot1</td><td>0.973</td><td>0.188</td></tr><tr><td>Lot2</td><td>0.979</td><td>0.162</td></tr><tr><td>Lot3</td><td>0.989</td><td>0.111</td></tr></table></td><td>Linear regression analysis of comparison study between A1CNow+ and Tosoh A1c 2.2 Plus
<table><tr><td>Slop</td><td>Intercept</td></tr><tr><td>1.02</td><td>-0.23</td></tr></table></td></tr>
<tr><td>Analytical Specificity</td><td><table><tr><td>INTERFERENT</td><td>TEST CONCENTRATION</td></tr><tr><td>Bilirubin</td><td>60mg/dl</td></tr><tr><td>Triglyceride</td><td>900mg/dl</td></tr><tr><td>Hemoglobin</td><td>500 mg/dL</td></tr><tr><td>Acetaminophen</td><td>200 µg/mL</td></tr><tr><td>Ascorbic acid</td><td>30mg/dl</td></tr></table></td><td><table><tr><td>INTERFERENT</td><td>TEST CONCENTRATION</td></tr><tr><td>Bilirubin</td><td>20 mg/dL</td></tr><tr><td>Triglyceride</td><td>3000 mg/dL</td></tr><tr><td>Hemoglobin</td><td>500 mg/dL</td></tr><tr><td>Acetaminophen</td><td>80 µg/mL</td></tr><tr><td>Ascorbic acid</td><td>5 mg/dL</td></tr></table></td></tr>
</table>

Issue 1: Even though the Room Temperature Stability is different, but the performances between the proposed device within the stable period and the predicate device within the stable period are the same.

Issue 2: The A1c EZ 2.0 glycohemoglobin analysis system utilizes the boronate affinity lateral chromatography method to quantitatively measure the percentage of glycohemoglobinA1c (HbA1c) in total hemoglobin. A solid phase separation matrix in membrane contains both negatively charged groups and boronate groups. When buffer A which is acidic flows through the matrix membrane, positively charged hemoglobin (including glycohemoglobin and non-glycohemoglobin) bind to the negatively charged groups. When buffer B flows through and the pH turns basic, hemoglobin loses its positive charge and is released from the matrix. However, cis-diols of glycohemoglobin can bind with the boronate group and stays in the matrix. The device uses a photometer to measure the reflectance and calculate the ratio of the glycohemoglobin to the total hemoglobin.

A1cNow+'s work mechanism is immunoassay, which utilizes the specific recognition of antibodies to glycohemoglobin and non-glycohemoglobin respectively. Detection and quantification of HbA1c and normal hemoglobin are also achieved by measurement of reflectance by photometer.

Although the test method of A1c Ez 2.0 and A1cNow+ differs, both of the devices use photochemistry and reflectance measure to quantify the percentage of glycohemoglobin. According to the comparison study, their accuracy is similar to each other.

7. Non-clinical Testing

7.1 Test strip stability test

The test strip's stability was tested and the test results showed that A1c Ez 2.0 HbA1c test kit can keep stable in room temperature for at least eighteen months.

7.2 Traceability

The A1C EZ Glycohemoglobin Analysis System is certified with the National Glycohemoglobin Standardization Program (NGSP) and International Federation of Clinical Chemistry and laboratory medicine (IFCC).

7.3 Performance test-bench (Analysis Performance)

a) Precision and reproducibility

Internal precision

Precision studies in internal laboratory were performed according to CLSI EP5-A2. Sample from normal patient (Level 1, HbA1c% = 5.8%, all labeled value of blood sample used in this performance test were determined by Tosoh G8) and diabetic patient (Level 2, HbA1c% = 12.2%) were run in the precision study. The precision study was performed on 1 instrument over 20 consecutive days by using 3 lots of the test kits.

Results of internal precision tests (HbA1c % NGSP)

CV %	Lot 1		Lot 2		Lot 3		All lots combined	
	Level 1	Level 2	Level 1	Level 2	Level 1	Level 2	Level 1	Level 2
Within-run	3.0%	2.7%	3.4%	2.9%	3.3%	2.9%	3.2%	2.8%
Between-run	0.8%	0.5%	0.0%	0.0%	1.3%	0.0%	0.9%	0.0%
Between-day	2.1%	1.6%	1.1%	0.9%	0.0%	1.0%	0.0%	0.3%
Total	3.8%	3.1%	3.5%	3.0%	3.5%	3.1%	3.3%	2.8%

Results of internal precision tests (HbA1c mmol/mol IFCC)

CV %	Lot 1		Lot 2		Lot 3		All lots combined	
	Level 1	Level 2	Level 1	Level 2	Level 1	Level 2	Level 1	Level 2
Within-run	4.8%	3.2%	5.4%	3.5%	5.2%	3.6%	5.3%	3.4%
Between-run	1.3%	0.7%	0.0%	0.0%	2.1%	0.0%	1.4%	0.0%
Between-day	3.4%	1.9%	1.7%	1.1%	0.0%	1.2%	0.0%	0.5%
Total	6.0%	3.8%	5.6%	3.6%	5.6%	3.8%	5.8%	4.4%

External precision

In this study, repeatability and reproducibility of A1C EZ 2.0 test strips have been evaluated at 3 external clinical sites. 10 sets of A1C EZ 2.0 analyzers, 3 lots of test strips and 3 levels of K2-EDTA anticoagulated venous blood samples (level 1- 5.1%, level 2- 7.3%, level 3- 11.7%) were used. For each sample, every operator performed the tests in 2 runs (1 run per day, tests at each site were finished in two days) by 10 sets of A1C EZ 2.0 analyzers with 3 different lots of test strips. Totally 120 tests were performed at each site for each sample. The precision represented as CV and mean value by percentage are given as below:

Table: Total CV includes all sites, operators, meters and test strip lots

	Level	1	2	3
	N	360	360	360
% NGSP	MEAN	5.09	7.37	11.54
	CV	3.1%	2.7%	2.3%
mmol/mol IFCC	MEAN	32.2	57.1	102.6
	CV	5.3%	3.8%	2.8%

Table: CV calculated for test strip lots

	Strip Lot	1			2			3		
	Level	1	2	3	1	2	3	1	2	3
	N	120	120	120	120	120	120	120	120	120
% NGSP	MEAN	5.09	7.37	11.57	5.10	7.35	11.47	5.09	7.41	11.58
	CV	3.2%	2.8%	2.1%	3.1%	2.6%	2.3%	3.0%	2.6%	2.4%
mmol/mol IFCC	MEAN	32.1	57.0	102.9	32.3	56.8	101.9	32.2	57.5	103.0
	CV	5.5%	4.0%	2.5%	5.3%	3.7%	2.9%	5.2%	3.6%	2.9%

Table: CV calculated for sites

	Site	1			2			3		
	Level	1	2	3	1	2	3	1	2	3
	N	120	120	120	120	120	120	120	120	120
% NGSP	MEAN	5.04	7.29	11.49	5.06	7.43	11.57	5.11	7.40	11.56
	CV	3.0%	2.7%	2.5%	2.7%	2.5%	2.1%	2.9%	2.5%	2.2%
mmol/mol IFCC	MEAN	31.6	56.2	102.0	32.9	57.7	103.0	32.0	57.3	102.8
	CV	5.2%	3.8%	3.0%	5.0%	3.6%	2.6%	4.9%	3.5%	2.7%

Table: CV calculated for operators

	Operator	1			2			3		
	Level	1	2	3	1	2	3	1	2	3
	N	60	60	60	60	60	60	60	60	60
% NGSP	MEAN	5.04	7.28	11.45	5.05	7.30	11.52	5.18	7.47	11.56
	CV	3.0%	3.0%	2.4%	3.0%	2.3%	2.5%	2.8%	2.5%	2.1%
mmol/mol IFCC	MEAN	31.5	56.1	101.6	31.6	56.2	102.4	33.0	58.1	102.8
	CV	5.2%	4.2%	3.0%	5.2%	3.3%	3.1%	4.9%	3.5%	2.6%
	Operator	4			5			6		
	Level	1	2	3	1	2	3	1	2	3
	N	60	60	60	60	60	60	60	60	60

% NGSP	MEAN	5.15	7.40	11.59	5.10	7.44	11.55	5.09	7.35	11.57
	CV	3.0%	2.5%	2.2%	3.1%	2.7%	2.2%	3.0%	2.1%	2.4%
mmol/mol IFCC	MEAN	32.8	57.4	103.2	31.7	57.8	102.7	32.3	56.8	102.9
	CV	5.2%	3.6%	2.7%	4.8%	3.8%	2.5%	5.0%	3.0%	2.9%

b) Linearity and reportable range/detection limit

Linearity was evaluated according to CLSI EP06-A. The test results and linear regression analysis are given in Table 5.

Table 5: Linear regression analysis of linearity test

	Slope	Intercept	R	R2
A1C EZ 2.0 (HbA1c % NGSP)	1.0334	-0.1628	0.9995	0.9989
A1C EZ 2.0 (HbA1c mmol/mol IFCC)	1.0377	-1.4795	0.9995	0.9990

The reportable range / detection limit of A1C EZ 2.0 is 4%~14% NGSP or 20-130 mmol/mol IFCC

c) Analytical specificity

Anticoagulants:

The results show that K_2-EDTA, Heparin Sodium and Sodium fluoride have no significant interference on HbA1c determination by A1c EZ 2.0 HbA1c Test System. Lithium Heparin,Sodium Fluoride or K_2-EDTA venous whole blood are suitable to be used with the device.

General interference substance:

The following substances do not interfere with test result:

Interfering Substance Study	**Test Concentration**
Acetaminophen	200 mg/L
Acetylcysteine	1,663 mg/L
Acetylsalicylic acid	1,000 mg/L
Ampicillin	1,000 mg/L
Ascorbic acid	300 mg/L
Bilirubin, conjugated	600 mg/L
Bilirubin, unconjugated	600 mg/L
Cholesterol	10,000 mg/L
Cyclosporine A	5 mg/L
Doxycycline	50 mg/L
Glucose	10,000 mg/L
Glyburide	2 mg/L
Hemoglobin	500 mg/dL
Hemolysis (Hemolysate)	5,000 mg/dL
Ibuprofen	500 mg/L
Levodopa	20 mg/L

Metformin	40 mg/L
Metronidazole	200 mg/L
Phenylbutazone	400 mg/L
Rifampicin	64 mg/L
Salicylic acid	599 mg/L
Theophylline	100 mg/L
Triglyceride	9,000 mg/L
Rheumatoid factor	491 IU/mL

Hemoglobin variant interference

The results from the A1C EZ 2.0 Glycohemoglobin Analysis System show that there is no significant interference for Hemoglobin C (≤ 44.7%), Hemoglobin D (≤ 41.7%), Hemoglobin E (≤ 32.6%), Hemoglobin S (≤ 37.8%), and Hemoglobin F (≤ 14.7%)

8. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

8.1 Sample volume study:

The sponsor performed a study to verify the test strip minimum sample volume requirement and the test strip fill error requirement established for the HbA1c analyzer. Blood samples were tested at five sample volumes (0.5, 1.5, 3, 4 and 5.5μL). Results support the claimed sample volume of 2.5-4.5ul.

8.2 Test System operating conditions:

Operating conditions were evaluated for temperatures ranging from 50 ~104^{o}F (10°C-40°C) and relative humidity from 10% to 90%. The following temperature and relative humidity (RH) conditions were tested: 22°C and 40% RH, 11°C and 11% RH, 10°C and 90% RH, 38°C and 10% RH, 40°C and 90% RH. Protocol and acceptance criteria were provided and found to be acceptable. The results supported the Sponsor's claimed operating temperature from 50 ~104^{o}F and relative humidity range from 30% to 75%.

8.3 Infection Control Studies:

Disinfection efficacy studies were performed on the materials comprising the meter by an outside commercial testing laboratory demonstrating complete inactivation of hepatitis B virus (HBV) with the chosen disinfectant, Clorox Healthcare Bleach Germecidal Wipes (EPA Registraiton# 67619-12). Robustness studies were also performed to demonstrate that there was no change in performance or in external materials of the meter after 18250 cleaning and disinfection cycles with Clorox Healthcare Bleach Germecidal Wipes. The robustness studies were designed to simulate 5 years of multiple-patient use.

9. Accuracy

Internal comparison study was performed according to CLSI EP09-A2 to evaluate accuracy of A1c EZ 2.0. The A1c EZ 2.0 was compared with the reference HPLC device Tosoh HLC-723 G8 and the predicate device A1CNow+ in this study. Linear regression analysis results of the accuracy study are

given as below:

Linear regression analysis of internal method comparison study (Unit: %NGSP)

	VS Tosoh HLC-723 G8			VS A1CNow+		
	Lot 1	Lot 2	Lot 3	Lot 1	Lot 2	Lot 3
Slop	0.973	0.979	0.989	0.966	0.976	0.989
Intercept	0.188	0.162	0.111	0.203	0.152	0.079
R-square	0.985	0.984	0.985	0.963	0.967	0.971

Linear regression analysis of internal method comparison study (Unit: mmol/IFCC)

	VS Tosoh HLC-723 G8			VS A1CNow+		
	Lot 1	Lot 2	Lot 3	Lot 1	Lot 2	Lot 3
Slop	0.975	0.979	0.989	0.966	0.975	0.988
Intercept	1.326	1.266	0.957	1.431	1.127	0.652
R-square	0.985	0.984	0.985	0.963	0.967	0.971

10. Conclusions

Based on device comparison information and non-clinical bench testing, the proposed device is substantially equivalent to legally marketed predicate devices (K090413).