K131580

Tosoh Bioscience, Inc.

510(k) Summary

JAN 2 3 2014

Tosoh Bioscience, Inc.'s
Automated Glycohemoglobin Analyzer HLC-723G8

Submitter:

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Device Name:
Automated Glycohemoglobin Analyzer HLC-723G8

Classification Name:
Hemoglobin A1c Test System
Class II
PDJ
21 CFR 862.1373

Predicate Device:

K121291
Roche Diagnostics Corporation
COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay

510(k) Summary

Automated Glycohemoglobin Analyzer HLC-723G8

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Device Description:

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 is an automated High Performance Liquid Chromatography (HPLC) system that separates and reports stable A1c (sA1c) percentage in whole blood. The operational portion of the G8 is composed of a sampling unit, liquid pump, degasser, column, detector, microprocessors, sample loader, floppy disk drive unit, operation panel and a printer.

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 uses non-porous ion- exchange high performance liquid chromatography (HPLC) for rapid, accurate and precise separation of the stable form of HbA1c from other hemoglobin fractions. The G8 uses a cation exchange column and separates the usual hemoglobin components in the blood into six fractions, A1a, A1b, F, LA1c, sA1c, and A0. The separation is done by eluting the hemoglobins from the column with a stepwise elution of three elution buffers containing different salt concentrations. The result report includes a sample ID, date, percentage and retention time of each fraction, sA1c percentage and total A1 percentage (A1a + A1b + sA1c), along with a chromatogram of the elution pattern of the hemoglobin fractions. If a sample contains a hemoglobin variant, the column elutes the material depending upon its charge.

New Device Intended Use:

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 is intended for *in vitro* diagnostic use for the quantitative measurement of % hemoglobin A1c (HbA1c) (DCCT/NGSP) and mmol/mo hemoglobin A1c (IFCC) in whole blood specimens. This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes.

Substantial Equivalence:
Comparison between the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 and – the COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay

Similarities

Parameter	**Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 (k)071132 (k)131580**	**COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay (k)121291**
Intended Use	The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 is intended for in vitro diagnostic use for the measurement of hemoglobin A1c (HbA1c) in whole blood specimens. Hemoglobin A1c measurements are used in the clinical management of diabetes to assess the long-term efficacy of diabetic control. This test is to be used as an aid in diagnosis of diabetes and identifying patients who may be at risk for developing diabetes.	This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes The COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay is an in vitro diagnostics reagent system intended for quantitative determination of mmol/mol hemoglobin A1c (IFCC) and % hemoglobin A1c (DCCT/NGSP) in hemolysate or whole blood on the Roche COBAS INTEGRA 800 clinical chemistry analyzer
Specimen Type	Human Whole Blood	Human Whole Blood
Matrix	EDTA Whole Blood	EDTA, Li-Heparin, Na Heparin, NaF/K- Oxalate
Standardization	Certified via the National Glycohemoglobin Standardization Program (NGSP)	Certified via the National Glycohemoglobin Standardization Program (NGSP)
Linearity	Linearity was previously evaluated for this assay under k071132. The reportable range is 4.0% - 16.9%.	Linearity was previously evaluated for this assay under k072714. The reportable range is 4.2-20.1%
Interference	Substances were evaluated at two HbA1c levels (6.5% and ≥8% HbA1c) Lipemia Conjugated Bilirubin Unconjugated bilirubin Rheumatoid Factor Glucose Total Protein Ascorbic Acid Acetylsalicylic Acid	Substances were evaluated at two HbA1c levels (~6.5 and ~8.9% HbA1c) Lipemia Conjugated Bilirubin Unconjugated bilirubin Rheumatoid Factor Glucose Total Protein Ascorbic Acid Acetylsalicylic Acid

	Acetaldehyde	
Precision	HbA1c concentration values of approximately 5%, 6.5%, 8% and 12% Precision was determined to be 0.7 - 1.8% (total precision) and 0.3 - 0.9% (within run, precision).	HbA1c concentration values of approximately 5%, 6.5%, 8% and 10% The between-analyzer and between-lot precision was equal to or less than 1.5% for concentrations in the range of 5.3% to 12.1% HbA1c
Hemoglobin Variant Interference	HbA2, HbS, HbC, HbD, does not interfere with the assay.	HbA2, HbS, HbC, HbD, does not interfere with the assay.
Bias	Concentration and Bias: 6.0% -0.847% 6.5% -0.753% 7.0% -0.673%	Concentration and Bias: 5.2% 1.21% 6.5% 1.29% 8.0% 1.34%
Total Error – allowable bias 6%	Concentration and Total Error 5.0 5.8% 6.5 2.8% 8.0 3.0% 12.0 3.1%	Concentration and Total Error 5.2 4.2% 6.5 4.1% 8.0 4.1%

Differences

Parameter	**Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 (k)071132**	**COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay (k)121291**
Assay Principle	Ion-exchange HPLC	Quantitative turbidimetric inhibition immunoassay
Detection Method	Visible wavelength detector	Absorption spectrum and measured biochromatically.
Method Comparison	The method comparison study was conducted utilizing the Automated Glycohemoglobin Analyzer HLC-723G8 and the Primus model ultra2. r = 0.991 (Y = 0.996x + 0.073)	The method comparison study was conducted using utilizing the Roche COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay and the Tosoh Automated Glycohemoglobin Analyzer HLC-723G8. r = None Listed (Y = 1.015x + 0.015)
Hemoglobin Variant Interference	HbE does interfere with the assay.	HbF does interfere with the assay.

PERFORMANCE CHARACTERISTICS

Interference:

This interference study was developed according to the CLSI guideline Interference Testing in Clinical Chemistry (EP7-A2).

Interference studies were conducted on known concentrations of HbA1c. They were spiked with increasing amounts of the substances below. Interference was determined as a variance greater than the assigned value x 1.00 ± 5%.

Potential Interferent	Range tested	%A1c Concentrations	Concentration in which no significant interference was observed
Acetylated Hb	10 - 50 mg/dL	6.5 and 9.5	50 mg/dL
Albumin	500 - 5000 mg/dL	6.6 and 14.7	5000 mg/dL
Aldehyde Hb	5.0 - 25 mg/dL	6.3 and 12.6	25 mg/dL
Ascorbic Acid	3.0 - 25 mg/dL	6.4 and 10.8	25 mg/dL
Carbamylated Hb	5.0 - 25 mg/dL	6.5 and 9.8	25 mg/dL
Bilrubin C	2.0 - 21 mg/dL	6.5 and 14.3	21 mg/dL
Labile Hb	200 – 1000 mg/dL	6.4 and 10.3	1000 mg/dL
Lipemia	100 - 1000 mg/dL	6.4 and 14.1	1000 mg/dL
Rheumatoid Factor	110 - 550 IU/mL	6.3 and 12.6	550 IU/mL
Bilirubin F	2.0 - 18 mg/dL	6.5 and 14.3	18 mg/dL

Hemoglobin Variant Interference study

Hemoglobin Variant	Number of Samples at approximately 6% and ≥8%	% HbA1c reference values	$\bar{x}$ IFCC mmol/ml	% Variant	Interference
HbS	10	6.2	44	36.42	No
	10	9.8	78.1	29.49	No
HbC	10	6.7	47	36.54	No
	10	8.0	59.4	35.06	No
HbE*	10	6.9	N/A*	N/A*	Yes
	10	9.8	N/A*	N/A*	Yes
HbD	10	6.0	43.1	36.23	No
	10	8.5	66.9	35.70	No
HbF	10	7.0	56.5	24.38	No
	10	8.7	74	7.43	No
HbA2	10	6.59	47.1	13.9	No
	10	8.05	62.9	12.7	No

*The G8 has known HbE interference. When a sample is suspected to contain HbE, a flag will be displayed. The %HbA1c result will not be reported from the analyzer.

The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 has known Hemoglobin E (HbE) interference. When a sample is suspected to contain HbE a flag will be displayed. The HbA1c result will not be reported from the analyzer.

The percent relative bias from the reference method at low and high concentrations of %HbA1c in each sample is:

	Percent Relative Bias from Reference Method at Low and High Concentrations of %HbA1c Samples	
Hb Variant	~6.5 %HbA1c	≥8 %HbA1c
S	0	-5
C	5	-5
E	*Flag	*Flag
D	1	-3
A2	-2	-2
F	5	2

Precision:

The precision study was developed with reference to the CLSI protocol entitled: Evaluation of Precision Performance of Quantitative Measurement Methods (EP5-A2).

Precision was assessed by assaying four concentrations of unaltered EDTA whole blood specimens with each using 3 lots and 3 instruments. Estimates of total and within-run precision were obtained from measurements of 2 replicates in a single run, 2 times a day for 20 non-consecutive days for each specimen/reagent combination. This equaled a total of 40 runs and 80 determinants for each data set. There were three (3) data sets at HbA1c concentrations of approximately 5%, 6.5%, 8% and 12% for each specimen.

Within-run Precision

Intra-assay (within run) Precision

Sample	Mean (%)	Standard Deviation (%)	Coefficient of Variation (%)
EDTA Whole Blood 5% A1	4.98	0.04	0.86
EDTA Whole Blood 5% A2	5.00	0.05	1.00
EDTA Whole Blood 5% A3	4.93	0.03	0.68
EDTA Whole Blood 6.5% B1	6.50	0.02	0.29
EDTA Whole Blood 6.5% B2	6.51	0.02	0.35
EDTA Whole Blood 6.5% B3	6.44	0.03	0.44
EDTA Whole Blood 8% C1	7.89	0.02	0.26
EDTA Whole Blood 8% C2	7.90	0.03	0.32
EDTA Whole Blood 8% C3	7.81	0.03	0.34
EDTA Whole Blood 12% D1	11.90	0.02	0.18
EDTA Whole Blood 12% D2	11.89	0.03	0.23
EDTA Whole Blood 12% D3	11.79	0.03	0.27

Total Precision

Sample	Mean (%)	Standard Deviation (%)	Coefficient of Variation (%)
EDTA Whole Blood 5% A1	4.98	0.09	1.83
EDTA Whole Blood 5% A2	5.00	0.09	1.79
EDTA Whole Blood 5% A3	4.93	0.08	1.69
EDTA Whole Blood 6.5% B1	6.50	0.04	0.68
EDTA Whole Blood 6.5% B2	6.51	0.07	1.14
EDTA Whole Blood 6.5% B3	6.44	0.07	1.10
EDTA Whole Blood 8% C1	7.89	0.08	0.98
EDTA Whole Blood 8% C2	7.90	0.07	0.89
EDTA Whole Blood 8% C3	7.81	0.07	0.86
EDTA Whole Blood 12% D1	11.90	0.16	1.31
EDTA Whole Blood 12% D2	11.89	0.19	1.58
EDTA Whole Blood 12% D3	11.79	0.13	1.14

Correlation:

The methods comparison study was conducted with reference to the CLSI protocol entitled: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (EP9-A2-IR).

Comparative testing was conducted between samples which were analyzed on the Automated Glycohemoglobin Analyzer HLC-723G8 (candidate method) and Primus ultra2 (comparative method) analyzed by a secondary NGSP reference laboratory.

A total of 120 unaltered EDTA whole blood specimens were assayed in singleton. Frozen specimens were utilized for this study. The sample distribution is as follows:

Hemoglobin A1c level	Number of samples tested at each A1c Level	%samples tested
≤ 5%	5	4.2%
5 – 6%	15	12.5%
6 – 6.5%	30	25.0%
6.5 – 7%	30	25.0%
7 – 8%	20	16.7%
8 – 9%	10	8.3
> 9%	10	8.3%
Total samples	120	100%

Regression Analysis		
	Deming	**Regular**
Slope:	0.996 (0.971 to 1.021)	0.987 (0.962 to 1.012)
Intercept:	0.073 (-0.110 to 0.255)	0.139 (-0.043 to 0.321)
Corr Coef (R):	0.991	
Bias:	0.047 (0.657 %)	
Points (Plotted/Total):	120/120	
Result Ranges:	4.50% to 16.5%	

Total Error Near the Cutoff

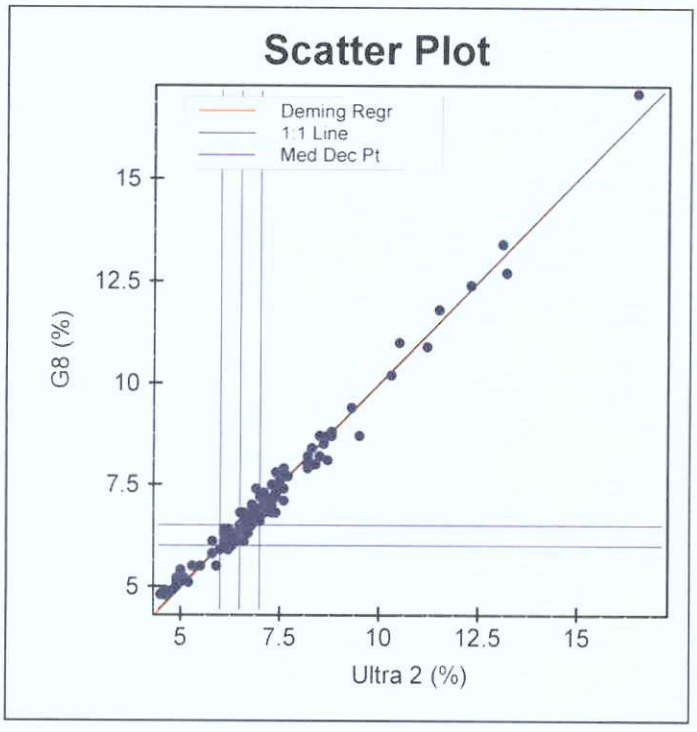
Using the results of bias estimation (%Bias) in the method comparison study and precision estimates in the precision study, Total Error (TE) at four concentrations: (5.0%, 6.5%, 8.0% and 12.0) was calculated as follows: %TE =|%Bias| + 1.96 *%CV*(1+%Bias). The results are presented in the tables below. %TE of ≤6% is acceptable.

Decision Level %	%Bias	%CV	%TE
5.0	1.08	1.84	5.8
6.5	0.75	0.68	2.8

8.0	0.54	0.98	3.0
12.0	0.24	1.31	3.1

Using the calculation: $(TE)_{95}$ = Bias + 1.96*SD the results are shown in the following table:

Decision Level %	Bias	SD	$(TE)_{95}$	Goal at 6%
5.0	0.054	0.09	0.23	0.30
6.5	0.049	0.04	0.13	0.39
8.0	0.043	0.08	0.20	0.48
12.0	0.029	0.16	0.34	0.72



Standards:

Number	FDA Recognition Number	Revision Date	Title
EP5-A2	7-110	10/31/2005	Evaluation of Precision Performance of Quantitative Measurement Methods: Approved Guideline- Second Edition
EP09-A2-IR	7-92	03/08/2004	Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline-Second Edition
EP7-A2	7-127	05/21/2007	Interference Testing in Clinical Chemistry; Approved Guideline - Second Edition

Linearity and Detection Limit:

Linearity was previously established for this assay under k071132. The reportable range for this device is 4.0-16.9% HbA1c.

Calibrator and Controls:

Calibrators (Tosoh A1c Calibrator Set) and Controls (Canterbury Scientific Hemoglobin A1c) are recommended for use with this device. The calibrators and controls were previously cleared under 510(k) numbers k071132 and k021484 respectively.

Traceability

The assigned HbA1c values of the Tosoh Automated Glycohemoglobin Analyzer are certified with The National Glycohemoglobin Standardization Program (NGSP). The NGSP certification expires in one year. See NGSP website for current certification at http://www.ngsp.org.

The final reportable result is traceable to both the International Federation if Clinical Chemistry (IFCC) and the Diabetes Control and Complications Trial (DCCT). The International Federation of Clinical Chemistry (IFCC) units of mmol/mol are calculated using the Master Equation NGSP (%) =0.09148 x IFCC (mmol/mol) + 2.52. HbA1c results are provided to the customers using two different units: NGSP equivalent units (%) and IFCC equivalent units (mmol/mol).

Conclusion:

The Tosoh Bioscience, Inc. Automated Glycohemoglobin Analyzer HLC-723G8 is substantially equivalent to the Roche Diagnostics Corporation, COBAS INTEGRA 800 Tina-quant HbA1cDx Gen.2 assay (k121291) for *in vitro* diagnostic use for the measurement of hemoglobin A1c (HbA1c) in whole blood specimens and to be used as an aid in diagnosis of diabetes and identifying patients who may be at risk for developing diabetes.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

January 23, 2014

TOSOH BIOSCIENCE, INC.
C/O ROBERT WICK
6000 SHORELINE COURT
SUITE 101
SOUTH SAN FRANCISCO CA 94080

Re: K131580
Trade/Device Name: Automated Glycohemoglobin Analyzer HLC-723G8
Regulation Number: 21 CFR 862.1373
Regulation Name: Hemoglobin A1c Test System
Regulatory Class: II
Product Code: PDJ
Dated: December 20, 2013
Received: December 20, 2013

Dear Mr. Wick:

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 Small Manufacturers, International and Consumer Assistance 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" (21CFR 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 Small Manufacturers, International and Consumer Assistance 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,

Courtney H. Lias -S

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 on last page.

510(k) Number *(if known)*
k131580

Device Name
Automated Glycohemoglobin Analyzer HLC-723G8

Indications for Use *(Describe)*
The Tosoh Automated Glycohemoglobin Analyzer HLC-723G8 is intended for in vitro diagnostic use for the quantitative measurement of % hemoglobin A1c (HbA1c) (DCCT/NGSP) and mmol/mo hemoglobin A1c (IFCC) in whole blood specimens. This test is to be used as an aid in diagnosis of diabetes and as an aid in identifying patients who may be at risk for developing diabetes.

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)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Stayce Beck

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