510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k071132

B. Purpose for Submission:

New device

C. Measurand:

Hemoglobin A1c (HbA1c) assay and calibrators

D. Type of Test:

Quantitative High Performance Liquid Chromatography

E. Applicant:

Tosoh Bioscience, Inc.

F. Proprietary and Established Names:

G8 Automated Glycohemoglobin Analyzer HLC-723G8

Hemoglobin A1C Calibrator Set

G. Regulatory Information:

1. Regulation section:

   21CFR Section 864.7470, Glycosylated Hemoglobin Assay

   21CFR Section 862.1150 Calibrator

2. Classification:

   Class II

3. Product code:

   LCP, JIS

4. Panel:

   Assay, Hematology (81)

   Calibrator, Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

The G8 Automated Glycohemoglobin Analyzer HLC-723G8 is intended for IN VITRO DIAGNOSTIC USE for the measurement of hemoglobin A1c (HbA1c) in whole blood specimens. A1c measurements are used in the clinical management of diabetes to assess the long-term efficacy of diabetic control.

The A1C Calibrator Set is a reference agent designed for calibrating Tosoh G8 Automated Glycohemoglobin Analyzer HLC–723G8.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Tosoh G8 Automated Glycohemoglobin Analyzer HLC-723G8

I. Device Description:

The Tosoh G8 Automated Glycohemoglobin Analyzer HLC–723G8 is an automated HPLC system that separates and reports stable A1C (sA1C) percentage in whole blood. The system consists of a sampling unit, liquid pump, degasser, column, detector, microprocessors, sample loader, floppy disk drive unit, operation panel and a printer.

The Hemoglobin A1c Calibrator Set contains five bottles each of Calibrators 1 and 2. The Calibrators contain processed human blood with a preservative. Human blood used in the preparation of the calibrator set has been tested and found to be negative for HBsAg, HIV and HCV.

The Hemoglobin A1c Control Set was cleared under k972265.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Tosoh G7 Automated HPLC Analyzer

2. Predicate 510(k) number(s):

k011434

3. Comparison with predicate:

Similarities/Differences		
Item	Device	Predicate
Intended Use	Quantitative measurement of A1c and Total HbA	Same
Methodology	Ion-exchange HPLC	Same
Standardization	Traceable to the Diabetes Control and Complication Trial (DCCT) reference method and IFCC. Certified via the National Glycohemoglobin Standardization Program (NGSP).	Same
Calibration	2 point	Same
Sample Type	Human anticoagulated (EDTA)whole blood	Same
Throughput (minutes)	1.6	2.2
Sample volume	4 uL	3 uL

K. Standard/Guidance Document Referenced (if applicable):

UL 6101-1 Electrical Equipment for Measurement, Control and Laboratory use – part 2-110: particular requirements for In Vitro Diagnostic (IVD) Medical Equipment

IEC 60601-1-2, (Second Edition 2001) Medical Electrical Equipment – Part 1-2: General Requirements for Safety: Electromagnetic Compatibility – Requirements and Tests

CEN EN 980:1996+A1:1999+A2:2001, Graphical Symbols for Use in the Labeling of Medical Devices (General)

BSN EN 375 Information Supplied by the Manufacturer with In Vitro Diagnostic Reagents for Professional Use

L. Test Principle:

The Tosoh G8 Automated Glycohemoglobin Analyzer HLC–723G8 uses a cation exchange column and separates the usual hemoglobin components in the blood into six fractions, A1a, A1b, F, L-A1c, SA1c and A0. The separation is done by eluting the hemoglobins from the column with a gradient of three elution buffers containing different salt concentrations.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Within-run precision was evaluated at two sites, one instrument per site. Each site was provided with the same sample set. The first study consisted of two levels of controls and three patient whole blood samples in the normal, high and very high %HbA1c range. Patient samples are EDTA human whole blood. The estimates of imprecision obtained from the analysis are given in the table below.

Samples	Number of Replicates	Mean(%HbA1c)	SD	%CV
Low Control	20	5.39	0.03	0.57
High Control	20	10.58	0.04	0.39
Whole Blood Normal	20	5.07	0.05	0.93
Whole Blood High	20	7.39	0.03	0.42
Whole Blood Very High	20	13.54	0.06	0.44

The second study consisted of diluted whole blood samples at low, high and very high %HbA1c values. The estimates of imprecision obtained from the analysis are given in the table below.

Samples	Number of Replicates	Mean(%HbA1c)	SD	%CV
Diluted Blood Low	20	6.1	0.06	1.0
Diluted Blood High	20	10.7	0.10	0.90
Diluted Blood Very High	20	13.0	0.13	1.0

Between-run precision was evaluated on five samples and two controls at two sites, one instrument per site. In the first study two controls and three whole blood samples, representing both normal and abnormal levels of %HbA1c were analyzed on 20 non-consecutive days. Each site was provided with the same sample set and directed to perform one sample per day on one instrument. The estimates of imprecision obtained from the analysis are given in the table below.

Samples	Number of Replicates	Mean(%HbA1c)	SD	%CV
Low Control	20	5.39	0.03	0.57
High Control	20	10.58	0.04	0.39
Whole Blood Normal	20	5.07	0.05	0.93
Whole Blood High	20	7.39	0.03	0.42
Whole Blood Very High	20	13.54	0.06	0.44

The second study at a different site consisted of diluted whole blood patient samples at low, and high %HbA1c values analyzed on 20 non-consecutive days. The estimates of imprecision obtained from the analysis are given in the table below.

Samples	**Number of Replicates**	**Mean(%HbA1c)**	**SD**	**%CV**
Diluted Patient Low	20	5.37	0.07	1.30
Diluted Patient High	20	10.52	0.07	0.60

b. *Linearity/assay reportable range:*

Linearity across the reportable range was performed using whole blood samples collected in EDTA with low (2.2%) HbA1c and high (16.9%) HbA1c levels. The observed values of the neat specimens were verified by HPLC. The theoretical value was calculated based upon mixing two samples at differing ratios and dividing by the dilution factor. The diluted samples were run in triplicate on the G8 Analyzer. The observed values were all within 100 ± 5% of the theoretical values. The results of the study are below.

Sample Pool	Observed %A1c	Theoretical % A1c	% Recovery
0	2.2		
1	3.6	3.6	100
2	5.1	5.1	100
3	6.6	6.6	100
4	8.0	8.1	98.8
5	9.4	9.6	97.9
6	11.2	11.0	101.8
7	12.4	12.5	99.2
8	14.0	14.0	100
9	15.5	15.5	100
10	16.9	16.9	100

A second linearity study was performed using four levels of commercially available linearity material tested in triplicate. The assigned values were compared to the mean of the observed values. The observed values were within ± 5% of the expected values for all samples tested. The results submitted demonstrated linearity across the claimed reportable range of 4.0 to 16.9 % A1c.

Control Level	Assigned Value %A1c	Mean of Observed Values	% Recovery
1	3.1	3.2	103.2
2	5.8	5.9	101.7
3	10.2	10.3	101.9
4	18.6	18.4	99.1

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*
Hemoglobin A1c reference materials were obtained from the Reference Material Institute for Clinical Chemistry Standards, Japan. The reference materials and calibrators were run on multiple G8 analyzers and other predicate Tosoh analyzers to assign Japanese Diabetic Society (JDS) A1c values to the calibrators. The JDS values are aligned to IFCC A1c values and NGSP A1c values according to an IFCC-JDS publication and the IFCC-NGSP Master Equation.

Real time stability and accelerated stability study protocols and acceptance criteria were reviewed and found to be acceptable to support stability of the Calibrators for two years at 2-8˚C.

d. *Detection limit:*

The reportable range is 4.0 to 16.9 % HbA1c. See the linearity study above for data on recovery of samples across the measuring range.

e. *Analytical specificity:*
Several interfering substance studies were performed which included Labile A1c, carbamylated A1c, icterus, lipemia, acetaldehyde, acetylsalicylic acid and EDTA. Whole blood pooled samples with normal and diabetic levels of HbA1c were initially analyzed without the spiked material. Then each sample was spiked with glucose, bilirubin, triglycerides, sodium cyanate, acetylsalicylic acid, acetaldehyde and EDTA to determine interference. The specification for interference was variance in the HbA1c value greater than the assigned value x 1.00 ± 0.05. No interference was seen from labile A1c up to 1000 mg/dL, icterus up to 20 mg/dL, lipemia up to 1000 mg/dL, carbamylated A1c up to 25 mg/dL, acetaldehyde up to 25 mg/dL, acetylsalicylic acid up to 50 mg/dL and EDTA up to 10 mg/dL.

A hemoglobin (Hb) variant interference study was performed using a high HbF human whole blood sample and commercially available controls for HbAE, HbAD, HbAS and HbAc. Two pooled whole blood patient samples representing normal and abnormal HbA1c levels were used. A dilution series of each variant Hb was prepared with the patient samples and measured on the Tosoh G8 Analyzer. The acceptance criteria were that a variant Hb is considered to interfere with the G8 Analyzer when the variance percent (%) or recovery percent (%) is greater than 100 ±10%. The results of this study show that HbAE was not distinguished from the other peaks and therefore does interfere with sA1c measurement. No interference was observed for HbF up to a concentration of 10%. No interference was observed for HbAD, HbAS and HbAC up to a concentration of 30%. Hemoglobins AD, AS, and AC elute after the A0 peak and are subtracted when calculating sA1c.

f. *Assay cut-off:*
Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

The manufacturer performed an in-house evaluation. Measurements for the Tosoh G8 analyzer were compared to the predicate, Tosoh G7 Analyzer on one hundred and fourteen EDTA whole blood samples. The range of samples on the new Tosoh G8 Analyzer was 4.0 to 16.8% A1c. A linear regression was performed resulting in a slope of 1.020, a y-intercept of -0.16 and a correlation coefficient of 0.998.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The sponsor conducted the Expected Values study in-house on EDTA whole blood samples collected from one hundred and forty-six apparently non-diabetic healthy adults representative of the U. S. population. The samples were tested on the G8 Analyzer and fell within the range of 4.4 – 6.1% A1c.

N. Instrument Name:

Tosoh G8 Automated Glycohemoglobin Analyzer HLC–723G8

O. System Descriptions:

1. Modes of Operation:

The HPLC is an automated system that consists of a sampling unit, liquid pump, degasser, column, detector, microprocessors, sample loader, floppy disk drive unit, operation panel and a printer.

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes ___X_____ or No _____

3. Specimen Identification:

The specimens are identified by a barcode.

4. Specimen Sampling and Handling:

   The samples are EDTA whole blood and are handled by the sampling unit.

5. Calibration:

   The analyzer performs a two point calibration

6. Quality Control:

   Two levels of external quality control materials are sold separately. The labeling instructs users to follow recommendations for running the quality per local, state and federal.

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

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.