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

A. 510(k) Number:

k170147

B. Purpose for Submission:

New device

C. Measurand:

Glycated Albumin

D. Type of Test:

Quantitative colorimetric assay

E. Applicant:

Asahi Kasei Pharma Corporation

F. Proprietary and Established Names:

Lucica Glycated Albumin-L

G. Regulatory Information:

1. Regulation section:

   21 CFR 864.7470

2. Classification:

   Class II

3. Product code:

   LCP - Assay, Glycosylated Hemoglobin

4. Panel:

   Hematology (81)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The Lucica Glycated Albumin-L is intended to be used for the quantitative measurement of glycated albumin in human serum on compatible clinical chemistry analyzers. The measurement of glycated albumin is useful for the intermediate term (preceding 2-3 weeks) monitoring of glycemic control in patients with diabetes. For in vitro diagnostic use only.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   Performance in the studies submitted in the 510(k) are based on the Roche/Hitachi Modular P Chemistry System.

I. Device Description:

The Lucica Glycated Albumin-L contains two glycated albumin reagents and two albumin reagents. The kit employs liquid reagents that do not require preparation. The glycated albumin reagent consists of GA R-1 (Pretreatment solution), GA R-2 (Enzymatic solution), ALB R-1 (pretreatment solution), and ALB R-2 (Coloring solution).

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Randox Laboratories Fructosamine

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

   k023763

3. Comparison with predicate:

Similarities		
Item	Candidate Device Lucica Glycated Albumin	Predicate Device Randox Fructosamine k023763
Intended Use	The Lucica Glycated Albumin-L is intended to be used for the quantitative measurement of glycated albumin in human serum. The measurement of glycated albumin is useful for the intermediate term (preceding 2-3 weeks) monitoring of glycemic control in patients with diabetes.	Same
Methodology	Enzymatic assay	Same
Sample Type	Serum	Serum or plasma

Differences		
Item	Candidate Device Lucica Glycated Albumin	Predicate Device Randox Fructosamine k023763
Analyte	Glycated albumin	Fructosamine
Analytical Range	173 - 979 mmol/mol	Up to 1734 µmol/L
Form	Liquid	Lyophilized

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

CLSI EP05-A3: Evaluation of Precision of Quantitative Measurement Procedures, 3rd Edition

CLSI EP06-A: Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach, 2nd Edition

CLSI EP07-A2: Interference Testing in Clinical Chemistry, 2nd Edition

CLSI EP09-A3: Measurement Procedure Comparison and Bias Estimation Using Patient Samples, 3rd Edition

CLSI EP15-A3: User Verification of Precision and Estimation of Bias, 3rd Edition

CLSI EP17-A2: Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures, 2nd Edition

L. Test Principle:

The Lucica Glycated Albumin-L provides quantitative measurement of glycated albumin based on an enzymatic method and quantitative albumin measurement by a colorimetric assay. The glycated albumin value (mmol/mol) is automatically calculated by the test system using the glycated albumin concentration (μmol/L) and the albumin concentration (μmol/L).

Measurement of glycated albumin:

The serum sample reacts with a ketoamine oxidase to eliminate endogenous glycated amino acids. The generated hydrogen peroxide is converted to H_2O by reaction with peroxidase and hydrogen donor (N, N-Bis (4-sulfobutyl)-3-methylaniline disodium salt). The treated solution reacts with an albumin-specific protease, which converts glycated albumin to glycated amino acids. The glycated amino acids react with a ketoamine oxidase to form glucosone, amino acids, and hydrogen peroxide. The generated hydrogen peroxide reacts with peroxidase in the presence of N, N-Bis (4-sulfobutyl)-3-methylaniline disodium salt and 4-aminoantipyrine (4-AA) forming a blue-purple pigment. Measurement of the absorbance of this blue-purple pigment quantifies the glycated amino acids produced by glycated albumin.

Measurement of albumin:

The serum sample reacts with the pretreatment solution to convert reduced albumin to oxidized albumin. The treated solution reacts with bromocresol purple, forming a blue conjugate of albumin and bromocresol purple. The absorbance of this blue conjugate is measured to quantify albumin concentration.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   An internal precision study and a multisite precision study at three centers were performed. Precision studies used three levels of glycated albumin (GA) controls, a human serum albumin (HSA) pool with a low glycated albumin value, and five native serum pools. For the internal precision studies, samples were tested with 2 runs per day, 2 replicates per run over 20 days. Results from different lots were similar.

   The precision summary table of glycated albumin values (mmol/mol) for the internal precision study is shown below.

Sample #	Sample Description	Mean (mmol/mol)	N	Repeatability		Within-Laboratory	
				%CV	SD	%CV	SD
1	Control L	280.1	80	0.7%	2.0	1.1%	3.0
2	Control H	649.8	80	0.6%	4.0	0.8%	5.2
3	High GA Control	999.5	80	0.6%	5.8	0.8%	7.8
4	Serum Pool	185.2	80	1.7%	3.1	2.2%	4.0
5	Serum Pool	228.0	80	0.8%	1.7	1.1%	2.6
6	Serum Pool	359.9	80	0.7%	2.6	0.9%	3.2
7	Serum Pool	877.7	80	0.8%	7.0	0.9%	7.8
8	Serum Pool	229.6	80	2.6%	6.0	3.3%	7.6
9	HSA Pool	120.4	80	0.8%	1.0	2.1%	2.5

Multi-site Precision Studies:

Multisite precision studies were performed at three laboratories. All three laboratories used the same samples, which included three native serum sample pools. Samples were assayed in replicates of five once daily for five days.

The multi-site precision summary table of glycated albumin values (mmol/mol) is shown below.

Sample Name	N	Mean (mmol/mol)	Repeatability		Within-Laboratory		Reproducibility	
			%CV	SD	%CV	SD	%CV	SD
Overall								
Serum pool 1	75	187.7	0.8	1.6	1.0	1.9	1.6	3.0
Serum pool 2	75	363.1	0.7	2.7	0.9	3.2	0.9	3.2
Serum pool 3	75	888.2	0.7	6.4	0.8	7.4	0.9	8.2

b. Linearity/assay reportable range:

Linearity studies were conducted to assess linearity of the glycated albumin value in mmol/mol. High and low glycated albumin native serum pools were mixed in different proportions to generate eleven target glycated albumin target values. Samples were tested in triplicate. The results for glycated albumin value (mmol/mol) linearity are shown in the table below:

Level	Target (mmol/mol)	Mean (mmol/mol)	Recovery
1	173	173.3	100.2%
2	290	291.0	100.3%
3	395	396.0	100.3%
4	491	491.3	100.1%
5	579	574.7	99.3%
6	659	664.7	100.9%
7	733	728.3	99.4%
8	802	798.3	99.5%
9	865	862.7	99.7%
10	924	913.7	98.9%
11	978	978.7	100.1%

The linear regression equation obtained was:

$y = 0.993\ x + 2.880$, $R^2 = 0.9998$

The claimed linear range of GA value 173 - 979 mmol/mol.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Traceability:

The Lucica Glycated Albumin calibrators and controls are traceable to Glycated Albumin Certified reference material JCCRM611, which is the reference measurement procedure and reference material for glycated albumin determination of the Japan Society of Clinical Chemistry.

Stability:

Protocols and acceptance criteria were reviewed for reagent shelf-life and found to be acceptable. The shelf-life for the Lucica Glycated Albumin reagents is 12 months when stored between 2 and 8 °C.

Sample stability:

Sample stability studies were performed and demonstrate that serum samples are stable for eight days at 2 - 8 °C, 24 months at -80°C, and six freeze/thaw cycles.

d. Detection limit:

Limit of Blank:

The Limit of Blank (LoB) determination was made using five blank samples that were measured in replicates of four for five days. Two reagent lots were used. The LoB was calculated as the mean of 95th and 96th ranked values. The claimed LoB for GA concentration is 6.9 µmol/L and 3.8 µmol/L for albumin concentration

Limit of Detection:

Eight low-level samples were measured in duplicate for five days using two reagent lots. The LoD was calculated using the parametric procedure specified by CLSI EP17-A2. The claimed LoD for GA concentration is 7.9 µmol/L and 7.0 µmol/L for albumin concentration.

Limit of Quantitation:

Eight low-level serum samples were analyzed in duplicate, twice daily over 14 testing days with two reagent lots. A precision profile curve as used to specify the GA or albumin concentration representing 10% CV as the limit of quantitation (LoQ). The claimed LoQ for GA concentration is 9.7 µmol/L and the claimed LoQ for albumin concentration is 21.8 µmol/L.

e. Analytical specificity:

Interference studies were performed using a normal serum pool and a diabetic serum pool. Six different concentration levels were prepared for each potential interferent by mixing high and low level interferent serum pools in varying proportions. Samples were analyzed in triplicate for glycated albumin concentration, albumin concentration, and glycated albumin value in a single run. The effect of albumin and total protein was evaluated by preparing specimens with high or low levels of albumin and total protein, and spiking glycated albumin at high and low levels. The level at which there is not significant interference (bias < ±10%) for each analyte with glycated albumin (mmol/mol) is listed in the table below.

Interferent	Concentration at Which No Significant Interference Observed
Albumin	7.8 g/dL
Bilirubin unconjugated	20.0 mg/dL
Bilirubin conjugated	20.0 mg/dL
Hemoglobin	288 mg/dL
Glucose	1000 mg/dL
Ascorbic Acid	100 mg/dL
Triglycerides	1516 mg/dL

Interferent	Concentration at Which No Significant Interference Observed
Uric Acid	1.40 mmol/L
Glibenclamide	0.66 µmol/L
Metformin Hydrochloride	310 µmol/L
Acetaminophen	1324 µmol/L
Acetylsalicylic Acid	3.62 mmol/L
Ibuprofen	2425 µmol/L
Hydroxyzine Dihydrochloride	2.67 µmol/L
Pravastatin Sodium	324.52 µmol/L
Penicillin G	29450 U/mL
Total protein	12.3 g/dL

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable.

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):

Peer-reviewed literature was provided to support the use of glycated albumin as a marker of glycemic control based on outcomes for microvascular complications, macrovascular complications, and prognosis in hemodialysis patients. Associations between glycated albumin and retinopathy and nephropathy have been identified in the Atherosclerosis Risk in Communities (ARIC) and Diabetes Control and

Complications Trial (DCCT) (1, 2). Elevated glycated albumin was associated with coronary heart disease and ischemic stroke in the ARIC cohort (3). In order to bridge the assay used in these clinical studies to the candidate device, a study was performed using n = 1831 samples that were measured by the candidate device and the research use only glycated albumin assay with a Roche Modular P Chemistry Analyzer. The performance of the Lucica Glycated Albumin-L assay showed good concordance (r = 0.997) with the research use only glycated albumin assay used in the literature.

1) Selvin E et al., Lancet Diabetes Endocrinol. 2014; 2(4): 279-88
2) Nathan DM, McGee P, Steffes MW, et al. Diabetes. 2014; 63(1): 282-290
3) Selvin E, Rawlings AM, Lutsey PL, et al. Circulation. 2015; 269-277

4. Clinical cut-off**:**

   Not applicable.

5. Expected values/Reference range:

   Healthy subjects (n = 262) with no history of diabetes were screened for diabetes using the oral glucose tolerance test and hemoglobin A1c. The reference range was based on the 2.5 to 97.5 percentiles for the glycated albumin of non-diabetic subjects. The glycated albumin reference range of non-diabetic subjects is 183 - 259 mmol/mol.

N. Proposed Labeling:

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

O. Conclusion:

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