510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k053253

B. Purpose for Submission:

Clearance for a new device

C. Measurand:

Albumin, Urine

D. Type of Test:

Quantitative, Turbidimetric Immunoassay

E. Applicant:

HemoCue AB

F. Proprietary and Established Names:

HemoCue Albumin 201 Analyzer

G. Regulatory Information:

1. Regulation section:

   21 CFR §862.2900, Automated Urinalysis System

   21 CFR §862.1645, Urinary protein or albumin (nonquantitative) test system

2. Classification:

   Class I, meets the limitation of exemptions, 862.9 (c), (5) and (9)

3. Product code:

   KQO and JIQ respectively

4. Panel:

   75, Chemistry

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The HemoCue Albumin is a quantitative rapid turbidimetric immunoassay of albumin in human urine using a specially designed analyzer, the HemoCue Albumin 201 System. The system is designed to be used for the quantitative determination of low levels of albumin in urine at the point of care for the purpose of screening for, diagnosing, monitoring and to supplement the clinical evidence in the treatment of microalbuminuria. The system is designed for testing using spot samples or timed collections. A quantitative result is obtained within 90 seconds. HemoCue Urine Albumin Microcuvettes are for in vitro diagnostic use only. The HemoCue Albumin 201 Analyzer is only to be used with the HemoCue Urine Albumin Microcuvettes.

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   HemoCue Albumin 201 Analyzer

I. Device Description:

The HemoCue Albumin 201 Analyzer system consists of a small, portable analyzer, software and plastic microcuvettes containing dried reagent (rabbit anti-human albumin antibody).

The HemoCue Albumin 201 Analyzer is factory calibrated against a turbidimetric method. The main parts are the cuvette holder (brings the microcuvette in the correct measuring position, vibrates the microcuvette to speed up the reaction), the optronic unit (performs a measurement of turbidity in the microcuvette), a display, power adaptor and embedded software.
The HemoCue Urine Albumin Microcuvette is made of polystyrene and contains a cavity that holds approximately 18 µL of specimen. The cuvette cavity contains the following reagents 11% w/w rabbit anti-human antibody (polyclonal), 355 w/w PEG, 18% w/w Tris/HCL-buffer, 2% w/w polymer and 33% w/w non-reactive ingredients.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Bayer Clinitek® 50 Urine Analyzer

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

   k960546

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Specimen Type	Urine	Urine
Clinical Use	Point-of-Care	Point-of-Care

Differences		
Item	Device	Predicate
Measuring Range	5-150 mg/L	10-150 mg/L
Device	Microcuvette	Strip
Result	Quantitative	Semiquantitative

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

CLSI/NCCLS EP6-A Vol. 23 No. 16, Evaluation of the Linearity of Quantitative Measurement Procedures
CLSI/NCCLS EP5-A2 Vol. 24 No. 25, Evaluation of Precision Performance of Quantitative Measurement Methods
CLSI/NCCLS EP9-A2 Vol. 22 No. 19, Method Comparison and Bias Estimation using Patient Samples
CLSI/NCCLS EP7-A Vol. 22 No. 27, Interference Testing in Clinical Chemistry

Electrical Safety:
IEC 60601-1 second edition 1988+A1:1991+A2:1995
EN 60601-1:1990+A1:1993+A2:1995

EMC:

Emission

EN 55 011:1998/A1:1999, radiated emission, Class B
EN 55 011:1998/A1:1999, conducted emission, Class B
EN 61 000-3-3:1995/A1:2001, Voltage fluctuations and flicker

Immunity

EN 61 000-4-2: 1995/A1:1998/A2:2001, Electrostatic discharge
EN 61 000-4-3: 2002/A1:2002, RF Electromagnetic discharge
EN 61 000-4-4: 1995/A1:2001/A2:2001, fast transients/burst
EN 61 000-4-5: 1995/A1:2001, surges
EN 61 000-4-6: 1996/A1:2001, RF conducted disturbances
EN 61 000-4-8: 1993/A1:2001, Power frequency magnetic field
EN 61000-4-11: 1995/A1:2001, voltage dips and interruptions

L. Test Principle:

The microcuvette contains dried reagents deposited on its inner walls. The urine sample is drawn into the microcuvette cavity by capillary action. The cuvette contains a specific rabbit anti-human albumin antibody (polyclonal) which forms an agglutinate with human albumin in the sample. The agglutination is enhanced by polymers. Within 90 seconds, the immunochemical reaction is completed and the turbidity is measured photometrically at 610 nm. The albumin concentration is proportional to the turbidity. When the end point is reached, the result is displayed in mg/L.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The within-run and total precision for urine albumin was estimated using the CLSI/NCCLS EP5-A method. The data represents samples run in duplicate, twice a day over 20 days on five instruments. Two levels of urine albumin control (Albutrol), low = 27 $\pm$ 9 and normal = 79 $\pm$ 23. The acceptance criterion is an SD $\leq$3 mg/L or CV $\leq$ 10% in the range 10-150 mg/L. The results are presented in the table below:

			Within-run		Total Precision	
Control Sample	N	Mean (mg/L)	SD (mg/L)	% CV	SD (mg/L)	% CV
1	400	27.9	2.41	8.6	2.58	9.2
2	400	81.8	3.20	3.9	3.48	4.3

b. Linearity/assay reportable range:

The linearity of the albumin measurement was demonstrated by comparing ten prepared urine samples on the HemoCue Albumin 201 System and a commercially available method. The predicted difference between the first order of regression and

the best-fitting order shall be less than 10 mg/L for albumin concentrations <10 mg/L and less than 15% for albumin concentrations 50-200 mg/L. The ten samples ranged in concentration from 0-200 mg/L. The method is linear from 0-200 mg/L with non-linearity less than 0.9 mg/L for albumin concentration 3.12 mg/L and less than 3.6% for albumin concentrations 50-200 mg/L. The measuring range of the assay is 7-150 mg/L.

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

The HemoCue Albumin 201 System is factory calibrated against a turbidimetric method with the calibration level traceable to the certified reference material CRM 470.

Shelf life Stability:

Three lots of the HemoCue Albumin cuvettes stored at 2-8 ºC, for the following time periods, one lot stored for 6 months, one at 9 months and the last for 12 months were used to assess stability. Artificial urine samples with the concentration 0, 25, 50 and 150 mg/L were assayed on each lot and each lot was assayed on five analyzers. Acceptance criteria are that the analytical performance is $\pm$ 20%, compared with the theoretical value for the artificial urine sample. All three lots showed analytical performance within the $\pm$ 20%. Shelf life was determined to be 9 months from the date of manufacture when stored at 2-8 ºC.

External control materials are recommended but not supplied.

d. *Detection limit:*

The limit of the blank of the assay was evaluated by testing 20 replicates of three individual urine samples and 60 replicates of a urine pool prepared from ten individual samples. Assay sensitivity is distinguishable with 95% confidence interval was determined to be 7 mg/L.

e. *Analytical specificity:*

Studies were performed to assess interference of different applicable chemical, protein and pH values. A substance was considered to show no interference if the results are within the clinical acceptable performance criteria $\pm$ 15%. Two urine samples at two different concentrations (25 and 75 mg/L) of albumin and two different pH values (4.5 and 9.0) were used to test interference. The following showed no interference at the concentrations tested:

Chemical or protein	Concentration
Acetoacetate	10 mmol/L
Acetone	120 mmol/L
Acetylsalicylic	0.5 g/L
Albumin	200-20,000 mg/L
Ascorbic Acid	0.5 g/L
Betanin	8 mg/L
Bilirubin	40 mg/L
B2-Microglobulin	1.0 mg/L
Calcium	0.016 mol/L
Creatinine	24 mmol/l
Glucose	110 mmol/L
Hemoglobin	2 g/L
IgG	15 mg/L
Potassium	180 mmol/L
Sodium	0.3 mol/L
Paracetamol	0.5 g/L
Urea	76-567 mmol/L
Uric Acid	0.35 mmol/L

f. Assay cut-off:

The 20 mg/L cutoff for the assay was evaluated by assaying 384 urine samples on the HemoCue 201 and a commercially available method. The results are in the table below:

		Reference Method		
		Positive	Negative	Total
Albumin, HemoCue 201	Positive	226	3	229
	Negative	2	153	155
	Total	228	156	384

The % agreement is 99%

2. Comparison studies:

a. Method comparison with predicate device:

One hundred and forty-three urine samples were tested on the HemoCue albumin 201 analyzer and a commercially available method. The range of the samples was 5-150 mg/L. The data yielded the following regression equation:

$y = 0.811x + .966$, $r = 0.977$

b. Matrix comparison:

Not applicable.

3. Clinical studies:

The performance was evaluated at three point-of-care sites by comparing 60 results, 20 per site obtained from the assistant nurse and the results obtained by a professional/trained user. The 60 samples were assayed in duplicate and the means of the samples were used to show correlation between the users. Acceptance criteria were a total difference less than 15% between the intended user and the trained professional user. The following regression equation was obtained.

y = 0.986X (professional user) + 0.750, r = 0.989

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable

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

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The following reference range was obtained from the literature:

Category	First morning spot sample (mg/L)	24-h collection (mg/24h)	Timed collection (ug/min)
Normal	<20	<30	<20
Microalbuminuria	20-200	30-299	20-199
Clinic albuminuria	>200	≥300	≥200

Literature referenced:

Rowe, D.J.F., Dawnay, A., Watts, G.F.: Microalbuminuria in diabetes mellitus: review and recommendations for the measurement of albumin in urine. Ann.Clin. Biochem. 27, 297-312 (1990)

N. Instrument Name:

HemoCue Albumin 201

O. System Descriptions:

1. Modes of Operation:

   Single-step

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:

   No patient ID entry. Samples are assayed one at a time.

4. Specimen Sampling and Handling:

   The microcuvette is manually filled and then insert into the cuvette holder on the instrument.

5. Calibration:

   Factory set

6. Quality Control:

   The HemoCue albumin 201 analyzer has an internal electronic self test of the optronic unit of the analyzer. When the analyzer is turned on the self test will automatically run. External quality control is recommended and to follow federal, state and local guidelines.

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.