

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

A. 510(k) Number:

k101089

B. Purpose for Submission:

New device

C. Measurand:

Urine microalbumin

D. Type of Test:

Quantitative immunoassay

E. Applicant:

Medica Corporation

F. Proprietary and Established Names:

EasyRA microALB Reagent, model number 10225

EasyRA microALB EasyCal, model number 10656

G. Regulatory Information:

1. Regulation section:

21 CFR § 866.5040, Albumin immunological test system

21 CFR § 862.1150, Calibrator

2. Classification:

Class II

3. Product code:

DCF, JIT

4. Panel:

Immunology (81), Chemistry (75)

H. Intended Use:

1. Intended use(s):

See indications for use below.

2. Indication(s) for use:

The EasyRA Microalbumin reagent is intended for the quantitative determination of microalbumin in human urine, using the MEDICA “EasyRA Chemistry Analyzer” in clinical laboratories. Microalbumin measurements using immunological tests aids in the diagnosis of kidney diseases.

The EasyRA Microalbumin calibrator facilitates measurements of microalbumin on the EasyRA Chemistry Analyzer when used in conjunction with Medica’s microalbumin reagent. The microalbumin calibrator is used to establish points of reference that are used in the determination of values in the measurement of microalbumin in human urine.

3. Special conditions for use statement(s):

For prescription use. For *in vitro* diagnostic use.

4. Special instrument requirements:

EasyRA Chemistry Analyzer

I. Device Description:

The EasyRA Microalbumin reagent is a two reagent device consisting of R1: a buffer reagent with preservative, and R2: goat anti-human albumin antibody with buffers and preservative.

The EasyRA Microalbumin calibrator consists of six levels each containing 1.0 ml of human albumin in saline (20 mM Tris, 150 mM sodium chloride) containing different concentrations of microalbumin (0.0 mg/dL, 0.5 mg/dL, 1.0 mg/dL, 5.0 mg/dL, 10.0 mg/dL, and 30.0 mg/dL)

Calibrator material was tested and found negative for HBsAg, HCV, and HIV-1 antibodies by FDA approved methods. However, all products that contain human source material should be handled in accordance with good laboratory practices.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Microalbumin reagent set and Calibrators, Pointe Scientific

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

k023860

3. Comparison with predicate:

microALB Reagent:

Product Attribute	Medica microALB Reagent	Pointe Scientific microALB Reagent – k023860
Intended Use	Same	Clinical chemistry reagent used to provide a direct quantitative measurement of μ ALB in human urine, using an automated chemical analyzer
Sample	Urine	Urine
Reagent type	Liquid ready-for-use	Liquid ready-for-use
Linearity range	0.5-30 mg/dL	0.5-30 mg/dL
Wavelength	340 nm and 700 nm	340 nm and 700 nm
Reaction type	End Point	End Point
Reagent storage	2 – 8 ⁰ C	2 – 8 ⁰ C
Test Methodology	same	When a sample is mixed with anti-human albumin goat antiserum, agglutination is caused by the antigen-antibody reaction. The turbidity is measured at 340 nm and 700 nm and albumin in the sample is quantitatively determined. The concentration of μ ALB in unknown samples is derived from a calibration curve using a Spline Curve fitting routine

microALB Calibrator:

Product Attribute	Medica microALB Multi-Calibrator	Pointe Scientific microALB Multi-Calibrator k023860
Intended Use	Same	The μ ALB multi-calibrator set is intended to be used for the calibration of the manufacturer's Microalbumin immunoturbidimetric assay for quantifying albumin in urine specimens.
Reagent storage	Same	2 – 8 °C
Test Methodology	Same	The calibrator is used to establish the calibration by using a spline curve fitting routine using a know concentration reagent and the measured absorbance. The calibration factor is used to determine the μ ALB concentration in the patient sample.

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

CLSI EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline-Second Edition, vol. 25, no. 25

CLSI EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical approach; Approved Guideline, vol. 23, no. 16

CLSI EP7-A2: Interference Testing in Clinical Chemistry; Approved Guideline-Second Edition, vol.25, no. 27

CLSI EP9-A2: Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline – Second Edition, vol. 22, no. 19.

CLSI EP17-A (modified): Determination of Limits of Detection & Limits of Quantitation

CLSI EP10-A2: Preliminary Evaluation of Quantitative Clinical Laboratory Methods

L. Test Principle:

When a sample is mixed with anti-human albumin goat antiserum, turbidity is caused by the antigen-antibody reaction. The turbidity is measured at 340nm and 700nm and albumin in the sample is quantitatively determined. The concentration of microalbumin in unknown samples is derived from a calibration curve using a Spline Curve fitting routine.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Two control materials and a third level created in-house by spiking a urine solution were evaluated in duplicate twice a day for 20 days on the EasyRA analyzer and analyzed according to CLSI EP5-A2. Results are summarized below.

Statistics of the Precision Study		Level 1	Level 2	Level 3
Total Average of Tested QC material (mg/dL)		0.86	5.36	22.96
Within Run Precision Stats	S _{wr}	0.02	0.06	0.48
	CV _{wr}	2.56%	1.14%	2.10%
Total Precision Stats	St	0.03	0.17	0.94
	CV _t	3.79%	3.11%	4.09%
Day-to-Day Precision Stats	S _{dd}	0.02	0.15	0.78
	CV _{dd}	2.64%	2.79%	3.39%
Run-to-Run Precision Stats	S _{rr}	0.008	0.04	0.21
	CV _{rr}	0.91%	0.77%	0.93%

b. *Linearity/assay reportable range:*

1) Linearity was determined using the guidelines provided by CLSI EP6-A on the EasyRA analyzer to evaluate the degree of non-linearity across the measuring range of the device. MicroALB linearity was evaluated using a commercially available urine chemistry validation verification test set. The highest and lowest level solutions were value assigned on the Cobas-Mira using the predicate reagent. The samples ranged in concentration from 0.36 to 32.36 mg/dL. A set of linearity solutions was prepared by diluting the high concentration solution with the low concentration. Each level was assayed in duplicate. The polynomial method was used for determining linearity.

The regression analysis statistic resulted in a 1st order regression equation of $Y = 0.9830 * X + 0.0629$, and a correlation coefficient = 0.9992. The 95% confidence interval for the 1st order slope is 0.9830 ± 0.0164 and for the 1st order intercept it is 0.0629 ± 0.2583 . The standard error is 0.346.

The reportable range of the assay is 0.5 to 30 mg/dL.

- 2) Extended range recovery studies were performed using albumin negative human urine samples spiked with 284.1 mg/dL, 257.4 mg/dL, 196.12 mg/dL, 129.93 mg/dL, 74.5 mg/dL and 39.13 mg/dL human albumin. The samples were diluted ten-fold with reagent grade deionized water using precise volumetric methods. These were used as the reference solutions that were analyzed on the EasyRA and the reported values were 1/10th the original (pre-diluted) values. Thus, the EasyRA results multiplied by ten provided the reference value of the original spiked solutions. The same spiked solutions were also run using the “ReRun” mode on the EasyRA. The results were compared to the ones calculated from the manually diluted solutions. The percent recovery was calculated using the observed versus expected values. The percent recovery of the spiked albumin samples fell within the 95% to 105% range. A dilution correlation factor was calculated to be 0.99 which is permanently inscribed parameter on the RFID tag of the reagent for the urine microalbumin assay. Based on this study, the range (0.5 to 30 mg/dL) can be extended to 300 mg/dL.
- 3) High dose hook effect was evaluated by spiking normal human urine with human serum albumin to obtain concentrations ranging from 100 mg/dL to 20,000 mg/dL. A hook effect (prozone) is observed above 400 mg/dL albumin concentration. Labeling recommends that urine samples be prescreened for high levels of protein by an alternative method and that samples with grossly elevated protein levels should not be assayed for microalbumin on the EasyRA analyzer.

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

Traceability:

The calibrator materials were cleared under k023860. The sponsor re-labels the calibrator vials from the manufacturer. The sponsor has provided a certificate of analysis from the manufacturer. In addition, the sponsor has provided inspection procedure for verification of new calibrator materials using the original calibrator materials and an existing pre-qualified lot of microalbumin reagent.

Calibrator Stability:

The stability of the calibrator for unopened and opened vial is performed by the manufacturer. The open vial stability at 2 to 8°C is 30 days.

Reagent Stability:

Real-time unopened reagent stability testing was performed at 2 to 8°C and is ongoing. The shelf life of the unopened reagent set is 24 months when stored at 2 to 8°C.

The on-board reagent stability study was evaluated for more than 30 days. The preset acceptance criterion was that the average result on day 15 and day 31 for each duplicate must be within $\pm 10\%$ of the average result for each duplicate from day 1. The reagent is stable on-board in the refrigerated reagent area of the Medica EasyRA Chemistry Analyzer for 30 days which is programmed on the RFID chip on the reagent wedge. The labeling recommends open vial storage at 2 to 8°C.

d. Detection limit:

The Limits of Blank, Limits of Detection, and Limits of Quantitation (LoB, LoD, LoQ) were determined following CLSI EP-17A on an EasyRA analyzer. The LoB was determined by using the zero calibrator (20mM Tris, 150mM sodium chloride), analyzed 20 times each over 5 days (n=100) using one lot of reagents. The LoB value of 0.02 mg/dL for the microalbumin assay was determined as the average of the 95th and 96th ranked value.

The Limit of Detection was determined by analyzing five urine samples with estimated microalbumin values in the range of 0.02 to 0.5 mg/dL on an EasyRA analyzer in quadruplicate each over 5 days (N = 20). The average SD of all five samples was subsequently used, in conjunction with the previously calculated LoB to determine LoD in the formula $LOD = LOB + C\beta *SDs$. The LoD is calculated to be 0.074.

The Limit of Quantitation was determined by analyzing 5 samples with known microalbumin concentrations ranging from 0.2 to 0.5 mg/dL in five different runs. Based on this study a value of 0.33 mg/dL for LoQ was predicted. Five independent solutions at 0.33 mg/dL in urine were analyzed in duplicate in 6 runs (N = 60), and calculating the means, standard deviations and coefficients of variation. The LoQ was determined to be 0.34 mg/dL where the overall CV was 6.91%, SD = 0.023 and total error was 0.05 mg/dL.

Limit of Blank (LoB)	0.02 mg/dL
Limit of Detection (LoD)	0.074 mg/dL
Limit of Quantitation (LoQ)	0.34 mg/dL

Lower reportable limit for the urine microalbumin assay on EasyRA analyzer is 0.5 mg/dL.

e. Analytical specificity:

Studies were performed on EasyRA analyzer according to CLSI EP7-A2. Normal human urine with added human serum albumin was used as the base material for the studies. A low level (~ 1.0 mg/dL) and high level (~10 mg/dL) pool were spiked with several different concentrations of endogenous and exogenous substances. Bias was determined by testing a control sample without the interferences and comparing it to the value obtained from a test sample containing the interfering compounds. Recoveries within $\pm 10\%$ of

the control sample were determined to have no significant interference. There was no significant interference detected up to the following concentrations of endogenous and exogenous substances at 2 levels of microalbumin:

Substance	No significant Interference within $\pm 10\%$ up to	
	Microalbumin at 10 mg/dL	Microalbumin at 1.0 mg/dL
Hemoglobin	100 mg/dL	100 mg/dL
Bilirubin	23.6 mg/dL	23.6 mg/dL
Ascorbic Acid	250 mg/dL	250 mg/dL
Glucose	560 mg/dL	560 mg/dL
Calcium	200 mg/dL	200 mg/dL
Creatinine	800 mg/dL	800 mg/dL
Urea	10 g/dL	10 g/dL
Uric Acid	150 mg/dL	75 mg/dL
Acetone	350 mg/dL	700 mg/dL
Urobilinogen	50 mg/dL	30 mg/dL
Kappa Light Chain	50 mg/dL	50 mg/dL
Lambda Light Chain	50 mg/dL	30 mg/dL
Furosemide	800 μ g/mL	800 μ g/mL
Trichloromethiazide	50 μ g/mL	50 μ g/mL
Acetaminophen	0.5 mg/mL	0.5 mg/mL
Ibuprofen	5 mg/mL	5 mg/mL
Glybenclamide	30 μ g/mL	30 μ g/mL
Metformin HCl	8 μ g/mL	8 μ g/mL

In addition, the labeling suggests that other compounds/drugs may interfere with the urine microalbumin assay on the EasyRA analyzer. Consult “Effects of Drugs on Clinical Laboratory Tests”, D.S. Young, AACC Press, 5th edition or later.

f. Assay cut-off:

Not applicable. This is a quantitative assay.

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison of the EasyRA microalbumin assay was performed on EasyRA analyzer and the predicate Pointe Scientific microalbumin assay on Cobas Mira analyzer. A total of 91 fresh urine samples were analyzed in singlicate on EasyRA analyzer and compared to the average of duplicate readouts on Cobas Mira analyzer. Sample values ranged from 0.62 mg/dL to 28.72 mg/dL. Regression correlation results are:

Slope: 1.0081 95% Confidence Interval: 1.0081 ± 0.0108
Intercept: 0.0117 95% Confidence Interval: 0.0117 ± 0.1218
R²: 0.9974 Std. Error: 0.3634

The measuring range of the assay is 0.5 mg/dL to 30.0 mg/dL.

b. Matrix comparison:

Not applicable - This device is for urine only.

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:

In the labeling the expected value for Microalbumin is stated as 30-300 mg/24 hours based upon literature⁶. Microalbumin concentrations of random urine specimens should be expressed as albumin-to-creatinine ratio⁵. Also, the sponsor recommends that each laboratory establish its own range of expected values, since differences exist among instruments, laboratories and local populations.

⁵ Tietz, N.W. (Ed), Fundamentals of Clinical Chemistry, 6th Ed.), W.B. Saunders C., Toronto, p398-399 (2008).

⁶ Stephenson, J.M., et al (1995) Diab. Med. 12:149-155.

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.