

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

**A. 510(k) Number:**

k091486

**B. Purpose for Submission:**

New device

**C. Measurand:**

Urine microalbumin

**D. Type of Test:**

Quantitative immunoassay

**E. Applicant:**

Kamiya Biomedical Company

**F. Proprietary and Established Names:**

K-Assay® Microalbumin

K-Assay® Microalbumin Calibrator

**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 K-Assay® Microalbumin reagent is for the quantitative determination of human albumin in urine by immunoturbidimetric assay. Measurement of albumin in urine aids in the diagnosis of kidney dysfunction. For in vitro diagnostic use.

The K-Assay® Microalbumin Calibrator is for the calibration of the K-Assay® Microalbumin assay for quantifying albumin in urine specimens. For in vitro diagnostic use.

3. Special conditions for use statement(s):

For prescription use.

4. Special instrument requirements:

Roche Hitachi 917

**I. Device Description:**

K-Assay® Microalbumin reagent is a two reagent device consisting of R1: a buffer reagent, and R2: goat anti-human albumin with buffers and preservatives.

The K-Assay® Microalbumin Calibrators are comprised of human albumin in known concentrations. A diluent containing no albumin is also included. There are 6 levels spanning the range from 0.0 mg/dL to 30.0 mg/dL. Calibrators are packaged separately from the reagent.

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:**

Device Name	Predicate device name	(k) number
K-Assay® Microalbumin reagent	Roche Tina-quant Albumin reagent	k932950
K-Assay® Microalbumin calibrators	Roche C.f.a.s. PUC calibrator	k050026

3. Comparison with predicate:

<b>Similarities and differences between the candidate device (K-Assay® Microalbumin reagent) and the predicate device (Roche Tina-quant Albumin reagent) - (k932950)</b>		
Item	Candidate device	Predicate
Indications for Use	Quantitative determination of human albumin in urine	Same
Intended use	Quantitative determination of human albumin in urine by immunoturbidimetric assay. Measurement of albumin in urine aids in the diagnosis of kidney dysfunction.	Quantitative determination of albumin in human urine on Roche automated clinical chemistry analyzers.
Assay principle	Immunoturbidimetric	Same
Turbidity wavelengths	340 nm (primary)/700 nm (secondary)	Same
Sample type	Urine	Same
Antibodies	Goat polyclonal	Sheep polyclonal
Range	0.2 to 30 mg/dL	0.3 to 40 mg/dL

<b>Similarities and differences between the candidate device (The K-Assay® Microalbumin Calibrators) and predicate device (Roche C.f.a.s. PUC calibrator)- (k050026)</b>		
Item	Candidate device	Predicate
Indications for use	Calibration of microalbumin	Same
Matrix	150 mM NaCl	20 mM HEPES
Levels	6 levels	5 levels
Analyte	Human albumin	Human albumin, human alpha-1 microglobulin, human IgG, human/sheep total protein
Form	Liquid, ready-to-use	Same
Volume	1 mL/vial	Same

**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.

**L. Test Principle:**

The K-Assay® Microalbumin reagent contains an anti-human albumin goat antiserum which, when mixed with the sample, results in turbidity due to the agglutination from the antigen-antibody reaction. Turbidity is measured at 340 nm and 700 nm. The amount of albumin in the sample is quantitatively determined by comparison to a standard calibration curve of known concentrations.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

Three control materials were evaluated in duplicate twice a day for 20 days on the Roche Hitachi 917 and analyzed according to CLSI EP5-A2. Results are summarized below.

	Mean	Within- Run	Between- Runs	Between- Day	Total				
	mg/dL	S.D.	CV%	S.D.	CV%	S.D.	CV%		
Control 1	0.793	0.025	3.099	0.006	0.719	0.016	1.963	0.030	3.738
Control 2	2.148	0.043	1.993	0.054	2.527	0.007	0.339	0.070	3.236
Control 3	5.883	0.108	1.838	0.063	1.079	0.038	0.649	0.131	2.228

In addition, three natural urine samples were collected and assayed using the protocol above at the lower and high ends of the measurement range. The summarized results are as follows:

	Mean	Within- Run		Between- Runs		Between- Day		Total	
	mg/dL	S.D.	CV%	S.D.	CV%	S.D.	CV%	S.D.	CV%
Sample 1	0.311	0.019	6.007	0.012	3.840	0.012	4.007	0.021	6.914
Sample 2	0.987	0.21	2.168	0.014	1.411	0.014	1.461	0.024	2.407
Sample 3	27.25	0.126	0.463	0.063	0.229	0.063	0.233	0.166	0.608

*b. Linearity/assay reportable range:*

- 1) Linearity studies were performed according to CLSI EP6-A on the Roche Hitachi 917 to evaluate the degree of non-linearity across the measuring range of the device. A human urine sample was spiked with human serum albumin to approximately 40 mg/dL. The spiked sample was serially diluted to prepare 12 test concentrations ranging from the LoQ (0.2 mg/dL) to 30 mg/dL. Testing was performed on one reagent lot, with each level being assayed in quintuplicate. Calculations were performed according to CLSI EP6-A. The observed concentration (y axis) was compared to the expected concentration (x axis). Linear regression with 95% confidence intervals (CI) is below. The correlation coefficient was 1.000.

		95% CI
Slope	0.9925	0.991-0.994
Intercept	0.0308	0.005-0.057

The reportable range of the assay is 0.2-30.0 mg/dL.

- 2) Recovery studies were performed using albumin negative human urine samples spiked with 100 mg/dL, 50 mg/dL, 40 mg/dL and 35 mg/dL human albumin. The samples were serially diluted 1:5 twice with each of the following diluents that are recommended in the labeling, i.e., isotonic saline with 0.05% Tween-20, isotonic saline, and deionized water. The dilutions were performed on the Roche Hitachi 917 analyzer using one lot of reagent in quintuplicate. Recovery was calculated using the observed versus expected values. All recoveries for all diluents yielded  $100 \pm 5\%$ .
- 3) High dose hook effect was evaluated by spiking normal human urine with human serum albumin to obtain concentrations ranging from 500 mg/dL to 3,000 mg/dL. The predetermined acceptance criterion is that the result is not less than the highest calibrator (30 mg/dL). There was no high dose hook effect up to 2,500 mg/dL. Labeling recommends diluting samples with results higher than the highest calibrator.

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

Traceability

A primary standard is gravimetrically prepared from human serum albumin and its true concentration is determined using the molecular extinction coefficient. This is compared to an in-house secondary standard. The reagent is calibrated using both sets of standards, analyzed on separate channels of an automated instrument. The %CV and recovery of the primary and secondary calibrators must meet the sponsor's predetermined acceptance criteria for release of the reagent.

New product calibrators are gravimetrically prepared at 5 levels using human serum albumin. The secondary calibrators are used to calibrate the microalbumin reagent. To validate the new calibrators, both the new calibrators and secondary calibrators are assayed as samples. The new calibrators must meet predetermined recovery values before being put into production. Target values for the product calibrators are 0.5 mg/dL, 1.0 mg/dL, 5.0 mg/dL, 10.0 mg/dL and 30 mg/dL. Diluent is used as a 0 mg/dL calibrator.

#### Reagent Stability

Real-time opened and unopened reagent stability testing was performed at 2-8°C, 25°C and 37°C. A new set of reagents was opened for each measurement at specified times. Calibrators and controls were stored at (-80°C) and new calibrator/controls were used for each measurement. Recoveries were compared and plotted versus the original values at time 0. The studies demonstrated that unopened reagent is stable for one year at 2-8°C, Opened reagent is stable for 30 days at 2-8°C.,

#### Calibrator Stability

Real-time opened and unopened calibrator stability testing was performed at 2-8°C, 25°C and 37°C. A new set of calibrators was opened for each measurement at specified times. Measurement values from the calibrators were compared to those from newly opened calibrators which had been stored frozen (-80°C). New reagent was used for each measurement. Recoveries were compared and plotted versus the original values at time 0. The studies demonstrated that unopened calibrators are stable for one year at 2-8°C. The labeling recommends storage at 2-8°C. Opened calibrators are stable for 30 days at 2-8°C. The labeling recommends open vial storage at 2-8°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 the Roche Hitachi 917. The LoB was determined by using a human urine sample with very low microalbumin levels, analyzed 20 times each over 5 days (n=100).

The Limit of Detection was determined by analyzing 6 human urine samples

diluted to a concentration in the range from the LoB to 4 times the LoB (0.03 mg/dL to 0.3 mg/dL) in quadruplicate over 5 days (n=120).

The Limit of Quantitation was determined by analyzing 10 samples with known concentrations ranging from the LoD to 0.50 mg/dL in replicates of 8 over 5 days and calculating the total error (bias  $\pm$  2SD), means, standard deviations and coefficients of variation. The LoQ was determined to be 0.2 mg/dL where the intra-assay CV was 9.8%, SD = 0.013 and total error was 0.097 mg/dL.

Limit of Blank (LoB)	0.03 mg/dL
Limit of Detection (LoD)	0.05 mg/dL
Limit of Quantitation (LoQ)	0.20 mg/dL

*e. Analytical specificity:*

Performed with Roche Hitachi 917

Studies were performed 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 (~ 1.73 mg/dL) and high level (~12 mg/dL) pool were spiked with 5 different concentrations of endogenous and exogenous substances. Bias was determined by testing a control sample without the interferents 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:

<b>Endogenous substances</b>	<b>No interference up to:</b>	<b>Exogenous substances</b>	<b>No interference up to:</b>
Bilirubin	66 mg/dL	Acetone	350 mg/dL
Calcium	160 mg/dL	Ascorbic acid	100 mg/dL
Creatinine	500 mg/dL	Furosemide	400 mcg/mL
Glucose	2,000 mg/dL	Triclormethiazide	20 mcg/mL
Hemoglobin	300 mg/dL	Acetaminophen	0.2 mg/mL
Urea	4,200 mg/dL	Ibuprofen	2.0 mg/mL
Uric acid	70 mg/dL	Glibenclamide	15 mcg/mL
Urobilinogen	20 mg/dL	Metformin Hydrochloride	4 mcg/mL
Kappa light chain	30 mg/dL		
Lambda light chain	30 mg/dL		

*f. Assay cut-off:*

Not applicable. This is a quantitative assay.

2. Comparison studies:

a. *Method comparison with predicate device:*

Performed with Roche Hitachi 917

Randomly collected natural urine samples were analyzed in singlicate comparing the Kamiya K-Assay to the predicate (n=91). Sample values ranged from 0.3 mg/dL to 30 mg/dL. The linear regression was  $y = 0.9149x + 0.0174$ ,  $r = 0.9963$ . The measuring range of the assay is 0.2 mg/dL to 30.0 mg/dL.

b. *Matrix comparison:*

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):

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Expected values  $< 2 \text{ mg/dL}^1$  or  $\leq 30 \text{ mg/24 hrs. (or } 0.03 \text{ g/day)}^2$

For spot A.M. samples, the expected values are:  $< 0.03 \text{ mg albumin/ mg creatinine}^2$

Microalbuminuria is defined as 30-300 mg albumin/24 hrs.<sup>2</sup>

Due to population differences, each laboratory should establish its own expected values using this kit.

Bibliography:

<sup>1</sup> Burtis, Carl A., et.al., Tietz Textbook of Clinical Chemistry and Molecular Diagnostics, 4th Edition (Elsevier Saunders, 2006), p. 547.

<sup>2</sup>Jacobs, David S. et al., Laboratory Test Handbook, 4<sup>th</sup> Edition (Lexi-Comp Inc, 1996), p. 643

**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.