

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

A. 510(k) Number:

k051191

B. Purpose for Submission:

New Device

C. Analyte:

Microalbumin

D. Type of Test:

Quantitative

E. Applicant:

Diagnostic Chemicals Limited

F. Proprietary and Established Names:

DCL Microalbumin Assay

G. Regulatory Information:

1. Regulation section:
21 CFR 866.5040
2. Classification:
Class II
3. Product Code:
DCF
4. Panel:
82 Immunology

H. Intended Use:

1. Intended use(s):
See indications for use below.
2. Indication(s) for use:
For the quantitative determination of low levels of albumin in urine.
For IN VITRO diagnostic Use.
Low levels of protein are normally excreted in the urine of healthy individuals. The uriniferous tubules and glomeruli filter out most of these excreted mucoproteins. Albumin, a protein of molecular weight of 50,000, is not easily filtered out and small amounts are excreted into the urine. Increased excretion of albumin (microalbuminuria) is an early indicator of glomerular disease.

Microalbuminuria is characterized by increased urinary excretion of albumin in the absence of overt nephropathy. Microalbumin is recognized as a strong predictor of impending nephropathy in Type I Diabetics and its mortality risk in diabetic patients. Early detection of microalbuminuria may be beneficial for treatment programs for diabetics because renal damage may be reversible if diabetes is well controlled at this stage.

Many of the methods traditionally used for measuring albumin lack the sensitivity and precision required for measuring microalbumin. The DCL Microalbumin Assay uses an immunoturbidimetric format which provides the sensitivity required for accurate determination of urinary microalbumin.

3. Special condition for use statement(s):

For prescription use only.

4. Special instrument Requirements:

Hitachi 717

I. Device Description:

The DCL Microalbumin assay is a dual reagent liquid assay. Reagent 1 consists of 20 mL of 100 mM tris (hydroxymethyl) aminomethane and preservatives. Reagent 2 consists of 10 mL of 20% solution of anti-human albumin, goat anti-serum, tris (hydroxymethyl) aminomethane and a preservative. The calibrators were previously cleared with PMN 510(k) submission (k991166).

J. Substantial Equivalence Information:

1. Predicate device name(s):

N-assay TIA Microalbumin

2. Predicate K number(s):

k934146

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For the quantitative determination of low levels of albumin in urine	For the quantitative determination of albumin in urine.
Turbidity Wavelengths	340 nm and 700 nm	340 nm and 700 nm
Sample	Urine	Urine
Differences		
Item	Device	Predicate
None		

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

Evaluation of the linearity of quantitative analytical methods- Second Edition. NCCLS Document EP6-P2, 2001
 Interference testing in clinical chemistry. NCCLS Document EP7-P, 1986.
 Method comparison and bias estimation using patient samples. 2nd ed. NCCLS Document EP9-A2, 2002.
 Evaluation of precision performance of clinical chemistry devices. NCCLS Document EP5-A, 1999.
 Quality Management Systems (Medical Devices). ISO Document 13485, 1998.
 Quality Management System. ISO Document 9001. 2000.

L. Test Principle:

A urine sample is mixed with the anti-human goat antiserum, agglutination is caused by the antigen-antibody reaction. The turbidity is measured at 340 and 700 nm and albumin in the sample is quantitatively determined.

M. Performance Characteristics (if/when applicable):1. Analytical performance:a. *Precision/Reproducibility:*

Within-run precision was conducted according to NCCLS EP5-A on two levels of urine controls (N=20) using the Hitachi 717. A low (normal) and a high (abnormal) level control were chosen. Run to run precision for the two urine control levels were conducted over 20 days (N=40). Two runs were analyzed (2 hours apart) daily using the Hitachi 717. Precision summary data is located in the following 2 tables.

Within-Run Precision

Level		Within-Run SD		Within-Run
mg/L	mg/dL	mg/L	mg/dL	%
5.79	0.579	0.8	0.028	4.8
44.95	4.495	1.75	0.175	3.9

Run-to-Run Precision

Level		Total SD		Within-Run
mg/L	mg/dL	mg/L	mg/dL	%
7.86	0.786	0.47	0.047	6.0
54.94	5.494	2.00	0.200	3.6

b. *Linearity/assay reportable range:*

Linearity was conducted according to NCCLS EP6-P2. Six samples were run in replicates of 4 and ranged from 0 to 310.38 mg/L using a previously cleared calibrator set. The assay demonstrated linearity

from 0 to 310.38 mg/dL. The sponsor chose 5 to 300 mg/L as its linear range for the DCL Microalbumin Assay.

The sponsor also conducted a pH and OD study. The results are in the table below.

	R1 Buffer reagent	Accepted Range	R2 Antibody reagent	Accepted Range
pH @ 25 C	7.58	7.0-8.0	7.45	7.0-8.0
OD @ 340 nm	0.023	<0.030	0.171	0.100-0.200

c. Traceability (controls, calibrators, or method):

The DCL Microalbumin Assay does not include controls or calibrators. The recommended K-Assay MicroAlbumin Multi-Calibrator Set was previously cleared under k991166. Spiked samples were spiked with commercially available human serum albumin.

Stability was determined using an accelerated heat stress study at two temperatures. Seven days at 37° C was equivalent to 24 months at 2-8° C storage. The sponsor claims 24 month reagent stability.

d. Detection limit:

The detection limit was determined according to NCCLS EP6-P. 10 sample water blanks resulted in a mean blank value of 0.02 mg/dL. 1 SD = 0.06 mg/dL, 3 SD = 0.18 mg/dL. The calculated lower limit of detection is 0.2 mg/L. However the sponsor chose 5 mg/dL as the lower limit of detection.

e. Analytical specificity:

Interference from icterus, lipemia, hemolysis and ascorbic acid were evaluated on the DCL microalbumin assay using the Hitachi 717 analyzer with a significance criterion of >10% variance from the control. A dose-response method was used for each interference substance- a control pool and test pool were prepared. The control pool and test pool had the same concentration of the microalbumin, but the test pool was spiked with intermediate levels of interference substance.

Significant lipemic interference was found at Intralipid levels from 0-1000 mg/dL (0-3000 mg/dL triglycerides) in a 14.1 mg/L (1.41 mg/dL) microalbumin sample.

Icterus levels of 0-684 µmol/L (0-40 mg/dL) were determined to have acceptable results up to 68.4 µmol/L (4 mg/dL) which had a 6.0% negative interference with a 16.8 mg/L (1.68 mg/dL) microalbumin sample.

Hemoglobin levels of 0-155 µmol/L (0-1000 mg/dL) were determined to have acceptable results up to 62.0 µmol/L (400 mg/dL) which has a 5.3% positive interference with a 17.1 (1.71 mg/dL) microalbumin sample.

There was no significant ascorbic acid interference found with ascorbic acid levels from 0-3000 µg/dL in a 18.3 mg/L (1.83 mg/dL) microalbumin sample.

f. Assay cut-off:
NA

2. Comparison studies:

a. Method comparison with predicate device:

Method comparison was conducted according to NCCLS EP9-A2. Sixty-four urine samples ranging from 0.0 to 197.4 mg/L were assayed using the Hitachi 717 on both the DCL Microalbumin Assay and the N-assay TIA Microalbumin. Both assays used the Nittobo multi-calibrator set. Linear regression analysis gave the following equation and a correlation coefficient of 0.9981.

$\text{N-Microalbumin Assay} = 0.949 \times (\text{DCL Microalbumin Assay}) + 0.36 \text{ mg/L}$
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b. Matrix comparison:

N/A. This is a urine only assay.

3. Clinical studies:

a. Clinical sensitivity:

N/A

b. Clinical specificity:

N/A

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

N/A

4. Clinical cut-off:

N/A

5. Expected values/Reference range:

The sponsor uses literature references for its expected value. The expected values of microalbumin were determined using 24-hour urine collected from 250 healthy donors. See package insert.

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.